

# NEOFAX<sup>®</sup>

## 2011

ANTI  
MICROBIALS

BIOLOGICALS

CARDIOVASCULAR

CNS DRUGS

DIURETICS

GI DRUGS

RESPIRATORY

MISCELLANEOUS

VITAMINS  
AND MINERALS

NUTRITIONALS



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Every effort has been made to ensure that the information herein, particularly that regarding dosage schedules, is accurate and in accord with good medical practice at the time of publication. However, because of ongoing research, changes in government regulations, experience, and the constant flow of information relating to drug therapy and drug reactions, changes in treatment and drug therapy occur.

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Thomson Reuters welcomes your inquiries, comments and suggestions for improvement.

#### Additions to this 24<sup>th</sup> edition:

- Dextrose
- Magnesium sulfate
- Penicillin G benzathine
- Penicillin G procaine
- Pneumococcal 13-valent conjugate vaccine (PCV13)
- Several new infant formulas added

#### Significant updates:

- Tall Man Letters applied to drug names based on ISMP recommendations
- Cefotaxime: Revised dosing
- Ceftriaxone: Revised dosing
- Enoxaparin: Added Black Box Warning
- Epinephrine: Revised dosing
- Flecainide: Added Black Box Warning
- Furosemide: Updated monograph
- Insulin: Revised dosing
- Intravenous Immune Globulin: Revised Preparations table
- Iron dextran: Added Black Box Warning
- Metoclopramide: Added Black Box Warning
- Octreotide: Revised dosing
- Propranolol: Revised dosing
- Protamine: Added Black Box Warning

#### Drug Concentrations and Compatibility Information References

Drug concentrations for injection/infusion are consistent with *Pediatric Injectable Drugs*, edition 9, 2010, edited by Phelps SJ, Hak EB and Crill CM. Compatibility information has been updated, and the primary reference is Trissel's *Handbook of Injectable Drugs*, edition 15, 2009. Both books are published by the American Society of Health-System Pharmacists. The major sources of product availability information are the individual package inserts.

#### Compatibility Terms and Definitions

In the Compatibility sections, the term "Dex/AA" is used instead of "TPN" to designate parenteral nutrition solutions that are similar to those used in neonates and contain dextrose, amino acids, and additives. For compatibility purposes, "terminal injection site" may be viewed as analogous to "Y-site injection" in adults. Terminal injection site in the neonate is meant to stress that it is important to infuse drugs as close to the patient as possible to provide effective drug delivery, for example at tri-fuse device attached to the IV catheter.





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The abbreviations listed below are used in the text.

a/A	arterial-alveolar (gradient)
a/ApO <sub>2</sub>	arterial-alveolar oxygen tension ratio
ABGs	arterial blood gases
ACTH	adrenocorticotrophic hormone
ALT	alanine aminotransferase
AMP	adenosine monophosphate
ANC	absolute neutrophil count
APTT	activated partial thromboplastin time
AST	aspartate aminotransferase
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
A-V	atrioventricular
BUN	blood urea nitrogen
BPD	bronchopulmonary dysplasia
bpm	beats per minute
CBC	complete blood count
CSF	cerebrospinal fluid
CHF	congestive heart failure
CNS	central nervous system
CVP	central venous pressure
DIC	disseminated intravascular coagulation
DNA	deoxyribonucleic acid
D <sub>5</sub> NS	5% dextrose in normal saline solution
DPPC	dipalmitoyl phosphatidylcholine
D <sub>5</sub> W	5% dextrose in water solution
D <sub>10</sub> W	10% dextrose in water solution
D <sub>15</sub> W	15% dextrose in water solution
D <sub>20</sub> W	20% dextrose in water solution
DT	diphtheria, tetanus [vaccine]
DTP	diphtheria, tetanus, pertussis [vaccine]
EEG	electroencephalogram
EKG	electrocardiogram
ET	endotracheal
FiO <sub>2</sub>	fractional inspired oxygen concentration
FRC	functional residual capacity
GABA	gamma-aminobutyric acid
GCSF	granulocyte colony stimulating factor
GE	gastroesophageal
GFR	glomerular filtration rate
GI	gastrointestinal
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immune globulin
HBsAg	hepatitis B surface antigen
Hib	Haemophilus influenzae b
HIV	human immunodeficiency virus

IC	intracardiac
IgG	immunoglobulin G
IM	intramuscular
IPV	inactivated polio vaccine (Salk)
IV	intravenous
IVH	intraventricular hemorrhage
IVIG	intravenous immune globulin (human)
Lf	potency of a given weight of an internationally accepted standard preparation of antiserum or antigen
LR	lactated Ringer's solution
NEC	necrotizing enterocolitis
NS	normal saline solution (0.9% sodium chloride)
OPV	oral polio vaccine
PMA	postmenstrual age
PCO <sub>2</sub>	partial pressure of carbon dioxide in the blood
PDA	patent ductus arteriosus
PO	by mouth (per os)
PO <sub>2</sub>	partial pressure of oxygen in the blood
ppm	parts per million
PR	by rectum
PVC	premature ventricular contraction
Q	every (quaque)
RDIs	Reference Daily Intakes (replaces US RDAs)
RDS	respiratory distress syndrome
RNA	ribonucleic acid
ROP	retinopathy of prematurity
S-A	sinoatrial node, "pacemaker" of the heart
subQ	subcutaneously
SGA	small for gestational age
SVT	supraventricular tachycardia
<sup>99</sup> Tc-IDA	technetium 99m-image display and analysis
TPN	total parenteral nutrition
TSH	thyroid-stimulating hormone
UAC	umbilical artery catheter
US RDAs	US Recommended Daily Allowances
VLBW	very-low-birth-weight



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# ANTIMICROBIALS

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## **An explanatory note about antimicrobial dosing charts:**

The antibiotic dosing charts reflect the fact that the renal function and drug elimination are most strongly correlated with Postmenstrual Age ("PMA", equivalent to Gestational Age plus Postnatal Age). Postmenstrual age is therefore used as the primary determinant of dosing interval, with Postnatal Age as the secondary qualifier.

Example: A baby born at 28 weeks gestation is now 21 days old. To determine the dosing interval for cefotaxime, first go to the row on the chart containing his Postmenstrual Age of 31 weeks (30 to 36), and then his Postnatal Age of 21 days (>14) to yield a dosing interval of 8 hours.

**Dose & Administration**

20 mg/kg per dose every 8 hours IV infusion by syringe pump over 1 hour. Prolong the dosing interval in premature infants less than 34 weeks PMA, or in patients with significant renal impairment or hepatic failure. Treat localized herpes simplex infections for 14 days, disseminated or CNS infections for 21 days.

**Chronic suppression:** 75 mg/kg per dose orally every 12 hours.

**Uses**

Treatment of neonatal herpes simplex infections, varicella zoster infections with CNS and pulmonary involvement, and herpes simplex encephalitis.

**Monitoring**

Periodic CBC. Serum concentrations two hours after a dose should be approximately 2 mcg/mL. Follow renal and hepatic function. Monitor IV site for phlebitis—if noted, make infusion solution more dilute.

**Adverse Effects/Precautions**

Neutropenia occurs in approximately 20% of patients - decrease dose or treat with G-CSF if ANC remains less than 500/mm<sup>3</sup>. Phlebitis may occur at IV site due to alkaline pH of 10. Risk of transient renal dysfunction and crystalluria is minimized by slow infusion rates and adequate patient hydration. Resistant viral strains may emerge during long-term therapy; these patients are at high risk for progressive life-threatening disease.

**Pharmacology**

Antiviral drug that is preferentially taken up by infected cells; inhibits viral DNA synthesis. CSF concentrations are 30 to 50% of serum concentrations. Oral absorption is 15 to 30%. Most of administered dose is excreted unchanged in urine, primarily via glomerular filtration. Protein binding and metabolism are minimal. Serum half-life is 3 to 4 hours in patients with normal renal and hepatic function.

**Special Considerations/Preparation**

Intravenous formulations available as solution (50 mg/mL) or as powder for solution in 500-mg and 1-g vials. Prepare powder for solution by dissolving contents of 500-mg vial in 10 mL sterile water for injection. Reconstituted solution is stable at room temperature for 12 hours. **Do not refrigerate.**

**Infusion solution concentration should be no greater than 7 mg/mL.** A 5-mg/mL dilution may be made by adding 1 mL of 50 mg/mL concentration to 9 mL of preservative-free normal saline. Dilution should be used within 24 hours.

Oral suspension available in 200 mg/5 mL concentration. Store at room temperature. Shake well before administration.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Solution Incompatibility:** Dex/AA.

**Terminal Injection Site Compatibility:** Amikacin, ampicillin, aminophylline, cefazolin, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, erythromycin lactobionate, famotidine, fluconazole, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, linezolid, lorazepam, magnesium sulfate, metoclopramide, metronidazole, milrinone, morphine, nafcillin, oxacillin, penicillin G, pentobarbital, piperacillin, potassium chloride, propofol, ranitidine, remifentanyl, sodium bicarbonate, theophylline, ticarcillin, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, and zidovudine.

**Incompatibility:** Fat emulsion. Aztreonam, caffeine citrate, caspofungin, cefepime, dobutamine, dopamine, meropenem, and piperacillin-tazobactam.

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- ◆ Product Information, Abraxis Pharmaceutical Products, 2006
- ◆ Product Information, GlaxoSmithKline, 2005

References updated 12/2010

Compatibilites updated 7/2009



**Dose & Administration**

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Chart**

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
≤29*	0 to 7	18	48
	8 to 28	15	36
	≥29	15	24
30 to 34	0 to 7	18	36
	≥8	15	24
≥35	ALL	15	24

\* or significant asphyxia, PDA, or treatment with indomethacin

**Uses**

Restricted to treatment of infections caused by gram-negative bacilli that are resistant to other aminoglycosides. Usually used in combination with a  $\beta$ -lactam antibiotic.

**Monitoring**

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

**Peak:** 20 to 30 mcg/mL (or  $C_{max}$ /MIC ratio greater than 8:1)  
(Draw 30 minutes after end of infusion, 1 hour after IM injection.)

**Trough:** 2 to 5 mcg/mL

**Suggested Dosing Intervals**

Level at 24 hrs (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤5	≈ 9	24
5.1 to 8.0	≈ 12	36
8.1 to 10.5	≈ 16	48
≥10.6		Measure level in 24 hours

continued...

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

**Pharmacology**

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a  $\beta$ -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of amikacin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

**Special Considerations/Preparation**

Available in concentrations of 50 mg/mL and 250 mg/mL. For IV use, dilute with a compatible solution to a concentration of 5 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, D<sub>20</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, aminophylline, amiodarone, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, enalaprilat, epinephrine, esmolol, fluconazole, furosemide, heparin (concentrations of 1 unit/mL or less), hydrocortisone succinate, hyaluronidase, linezolid, lorazepam, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, nicardipine, penicillin G, pentobarbital, phenobarbital, potassium chloride, ranitidine, remifentanyl, sodium bicarbonate, vancomycin, vitamin K<sub>1</sub>, and zidovudine.

**Incompatibility:** Fat emulsion. Amphotericin B, ampicillin, azithromycin, heparin (concentrations greater than 1 unit/mL), imipenem/cilastatin, mezlocillin, nafcillin, oxacillin, phenytoin, propofol, thiopental, and ticarcillin/clavulanate.

*continued...*

**Selected References**

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- ◆ Product Information, Bedford Laboratories, 2004

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

Monitoring, Compatibilities and References updated 3/2005



**Dose & Administration**

1 to 1.5 mg/kg every 24 hours IV infusion over 2 to 6 hours.

Dosage modification for renal dysfunction is only necessary if serum creatinine increases greater than 0.4 mg/dL from baseline during therapy - hold dose for 2 to 5 days. Alternate-day dosing recommended over decreasing daily dose in patients experiencing renal toxicity.

**Uses**

Treatment of systemic fungal infections and severe superficial mycoses.

**Monitoring**

Monitor CBC, electrolytes, urine output, BUN, and serum creatinine at least every other day. Observe IV site for irritation—phlebitis is common.

**Adverse Effects/Precautions**

Hypokalemia (serum  $K^+$  less than 3 mmol/L) and/or a transient increase in serum creatinine occurs in approximately 16% of treated patients. Renal blood flow and GFR may be decreased by 20% to 60%. Injures tubular epithelium with resultant urinary loss of potassium and magnesium, decreased reabsorption of sodium, and renal tubular acidosis. Sodium intake greater than 4 mEq/kg per day may prevent or decrease nephrotoxicity. Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills. Consider analgesia before beginning infusion. Cardiac arrest has occurred in patients who received 10 times the recommended dose.

**Black Box Warning**

According to the manufacturer's black box warning, it is recommended that the product name and dosage are verified if the prescribed dose exceeds 1.5 mg/kg.

**Pharmacology**

Amphotericin B binds to ergosterol in the membrane of sensitive fungi and may be fungicidal or fungistatic. The therapeutic concentration range is not well-defined. Highly protein-bound (greater than 90%). Elimination half-life is approximately 15 days. Drug may accumulate in tissues to a significant concentration and be excreted renally for months.

**Special Considerations/Preparation**

Available as powder for injection in 50-mg vials. Reconstitute using  $D_5W$  or Preservative free SW to a concentration of 5 mg/mL, then dilute further using  $D_5W$  to a concentration no greater than 0.1 mg/mL for infusion. Reconstituted solution stable for 24 hours at room temperature or 7 days in refrigerator. **Do not flush IV or mix amphotericin with saline solution** — precipitation will occur. May filter if necessary; mean pore diameter should not be less than 1 micron. **Protect from light.**

**Solution Compatibility:**  $D_5W$ ,  $D_{10}W$ ,  $D_{15}W$ , and  $D_{20}W$ .

**Solution Incompatibility:** Dex/AA solutions and NS.

**Terminal Injection Site Compatibility:** Amiodarone, heparin, hydrocortisone, sodium bicarbonate, and zidovudine.

*continued...*

**Incompatibility:** Fat emulsion. Amikacin, aztreonam, calcium chloride, calcium gluconate, cefepime, cimetidine, ciprofloxacin, dopamine, enalaprilat, fluconazole, gentamicin, linezolid, magnesium sulfate, meropenem, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanyl, and tobramycin.

### Selected References

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- ◆ Starke JR, Mason EL, Kramer WG, Kaplan SL: Pharmacokinetics of amphotericin B in infants and children. *J Infect Dis* 1987;155:766.
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- ◆ Product Information, Bristol-Myers Squibb, 2006.

Adverse Effects/Precautions and References updated 1/2010

Dose & Administration updated 7/2009

Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2005



**Dose & Administration**

5 mg/kg per dose every 24 hours IV infusion by syringe pump over 2 hours.

**Uses**

Treatment of systemic fungal infections resistant to conventional amphotericin B therapy or in patients with renal or hepatic dysfunction.

**Monitoring**

Serum amphotericin B concentrations are not routinely followed. Monitor urine output. Periodic CBC for thrombocytopenia, electrolytes for hypokalemia, BUN, serum creatinine, and hepatic transaminases.

**Adverse Effects/Precautions**

Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills.

**Pharmacology**

ABELCET® consists of amphotericin B complexed with two phospholipids in a 1:1 drug-to-lipid ratio. Acts by binding to the sterol component of a cell membrane leading to alterations in the cell wall permeability and death. Penetrates the cell wall of susceptible fungi. Concentrates in the liver and spleen. Less nephrotoxic than conventional amphotericin B. Mean serum half-life in adults 24 to 38 hours. The pharmacokinetics of amphotericin B lipid complex is nonlinear.

**Special Considerations/Preparation**

Available as a ready-to-use admixture containing 100-mg ABELCET® in 20-mL suspension (5 mg/mL). Shake the vial gently until there is no evidence of any yellow sediment on the bottom. Withdraw the appropriate dose into a syringe using an 18 gauge needle. Remove the needle and replace with the supplied 5 micron filter needle. Inject the drug into a different syringe containing a measured amount of D<sub>5</sub>W so that the **final infusion concentration is 1 to 2 mg/mL**. Shake until thoroughly mixed. Check for complete dispersion. The diluted admixture is stable for 48 hours refrigerated and an additional 6 hours at room temperature.

**Do not freeze. Protect from light.**

**Do not flush IV or mix ABELCET® with saline solutions - precipitation will occur.**

**Solution Compatibility:** D<sub>5</sub>W at 1 to 2 mg/mL dilution.

**Solution Incompatibility:** Dex/AA and NS.

**Terminal Injection Site Compatibility:** No available data.

*continued...*

**Selected References**

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- ♦ Walsh TJ, Seibel NL, Arndt C, et al: Amphotericin B lipid complex in pediatric patients with invasive fungal infections. *Pediatr Infect Dis J* 1999;18:702-708.
- ♦ Wong-Beringer A, Jacobs RA, Guglielmo BJ: Lipid formulations of amphotericin B: Clinical efficacy and toxicities. *Clin Infect Dis* 1998;27:603-618.
- ♦ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ♦ Product Information, Enzon, 2002

Compatibilities updated 7/2009

Dose and References updated 3/2007

**Dose & Administration**

5 to 7 mg/kg per dose every 24 hours IV infusion by syringe pump over 2 hours.

**Uses**

Treatment of systemic fungal infections resistant to conventional amphotericin B therapy or in patients with renal or hepatic dysfunction.

**Monitoring**

Serum amphotericin B concentrations are not routinely followed. Monitor urine output. Periodic CBC for thrombocytopenia, electrolytes for hypokalemia, BUN, serum creatinine, and hepatic transaminases.

**Adverse Effects/Precautions**

Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills.

**Pharmacology**

Ambisome® consists of amphotericin B intercalated within a single bilayer liposomal drug delivery system. Acts by binding to the sterol component of a cell membrane leading to alterations in the cell wall permeability and death. Penetrates the cell wall of susceptible fungi. Concentrates in the liver and spleen but penetrates the CNS less than conventional amphotericin B. Less nephrotoxic than conventional amphotericin B. Mean serum half-life in adults 24 to 38 hours. The pharmacokinetics of amphotericin B liposome is nonlinear.

**Special Considerations/Preparation**

Available as powder for injection in 50 mg vials. Reconstitute by adding 12 mL of sterile water for injection to a yield a concentration of 4 mg/mL. Immediately shake vial vigorously for 30 seconds. Check for complete dispersion. Reconstituted suspension stable for 24 hours refrigerated.

**Do not freeze. Protect from light.**

Before administration, Ambisome® must be diluted with D<sub>5</sub>W to a final concentration less than 2 mg/mL. A 1 mg/mL dilution may be made by filtering (using 5 micron filter) 1 mL of reconstituted solution into 3 mL of D<sub>5</sub>W. Use one filter per vial of Ambisome®. Use solution within 6 hours of dilution.

**Do not flush IV or mix Ambisome® with saline solutions-precipitation will occur.**

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, D<sub>20</sub>W, D<sub>25</sub>W.

**Solution Incompatibility:** Dex/AA and NS.

**Terminal Injection Site Compatibility:** No available data.

*continued...*

**Selected References**

- ◆ Juster-Reicher A, Flidel-Rimon O, Amitay M, et al: High dose liposomal amphotericin B in the therapy of systemic candidiasis in neonates. *Eur J Clin Microbiol Infect Dis* 2003;22:603-07.
- ◆ Scarcella A, Pasquariello MB, Giugliano B, et al: Liposomal amphotericin B treatment for neonatal fungal infections. *Pediatr Infect Dis J* 1998;17:146-148.
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- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Gilead Sciences, 2005.

Compatibilities updated 7/2009

References updated 3/2007

**Dose & Administration**

25 to 50 mg/kg per dose by IV slow push, or IM.

**Group B streptococcal infections:** Some experts recommend using 150 to 200 mg/kg per day for bacteremia and 300 to 400 mg/kg per day for meningitis, in divided doses at more frequent intervals. The addition of an aminoglycoside for initial therapy is also recommended.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Broad-spectrum antibiotic useful against group B *streptococcus*, *Listeria monocytogenes*, and susceptible *E coli* species.

**Monitoring**

Serum concentration can be measured but is not usually necessary.

**Adverse Effects/Precautions**

Very large doses may result in CNS excitation or seizure activity. Moderate prolongation of bleeding times (by approximately 60 seconds) may occur after repeated doses. Hypersensitivity reactions (maculopapular rash, urticarial rash, or fever) are rare in neonates.

**Pharmacology**

Ampicillin is a semisynthetic penicillin that is bactericidal. Clearance is primarily by the renal route and is inversely related to postnatal age. Serum half-life in term infants younger than 7 days is approximately 4 hours.

**Special Considerations/Preparation**

Available as powder for injection in 125-, 250-, 500-mg, 1-g, and 2-g vials. Reconstitute using sterile water for injection. Maximum concentration for IV infusion is 100 mg/mL. Mix to a final concentration of 250 mg/mL for IM administration. Reconstituted solution must be used within 1 hour of mixing because of loss of potency.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Solution Incompatibility:** Dex/AA.

continued...

**Terminal Injection Site Compatibility:** Fat emulsion. Acyclovir, alprostadil, aminophylline, aztreonam, calcium gluconate, cefepime, chloramphenicol, cimetidine, clindamycin, enalaprilat, famotidine, furosemide, heparin, hydrocortisone succinate, insulin, lidocaine, linezolid, magnesium sulfate, metronidazole, milrinone, morphine, phytonadione, potassium chloride, propofol, ranitidine, remifentanyl, and vancomycin.

**Incompatibility:** Amikacin, amiodarone, dopamine, epinephrine, erythromycin lactobionate, fluconazole, gentamicin, hydralazine, metoclopramide, midazolam, nifedipine, sodium bicarbonate, and tobramycin.

### Selected References

- ◆ Sheffield MJ, Lambert DK, Henry E, Christensen RD: Effect of ampicillin on the bleeding time of neonatal intensive care patients. *J Perinatol*, advance online publication 31 December 2009.
- ◆ Shaffer CL, Davey AM, Ransom JL, et al: Ampicillin-induced neurotoxicity in very-low-birth-weight neonates. *Ann Pharmacother* 1998;32:482-484.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
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- ◆ Axline SC, Yaffe SJ, Simon HJ: Clinical pharmacology of antimicrobials in premature infants: II. Ampicillin, methicillin, oxacillin, neomycin, and colistin. *Pediatrics* 1967;39:97.
- ◆ Product Information, Sandoz 2004.

Adverse Effects, References updated 1/2010

Dose & Administration, Compatibilities updated 7/2009

**Dose & Administration**

**Treatment and Prophylaxis of Pertussis infections:** 10 mg/kg per dose orally, once daily for 5 days.

Intravenous treatment is limited to those who cannot be treated orally. To date no clinical studies have been conducted to evaluate the safety or efficacy of IV azithromycin in the pediatric population. Suggested IV dose: 5 mg/kg per dose once daily.

**Prophylaxis of ophthalmia neonatorum (erythromycin ointment shortage only):** 1 to 2 drops of the 1% ophthalmic solution instilled in each conjunctival sac.

**Uses**

Treatment and postexposure prophylaxis against *Bordetella pertussis*. As a substitute for penicillin in situations of significant allergic intolerance.

In the event of an erythromycin ointment shortage, azithromycin ophthalmic solution is an alternative for prophylaxis of ophthalmia neonatorum.

**Monitoring**

Assess gastrointestinal tolerance.

**Adverse Effects/Precautions**

Limited data in neonates. Diarrhea and/or vomiting occur in 5% to 12% of patients. Irritability, rash, and blood in stool have also been reported. There is one new case report of pyloric stenosis in 2 of 3 triplets treated with azithromycin for pertussis.

**Pharmacology**

Azithromycin is classified as an azalide, a subclass of macrolide antibiotics. In vitro activity has been demonstrated against *Bordetella pertussis*, as well as Streptococci (Groups C, F, G and Viridans), *Ureaplasma urealyticum*, and Peptostreptococcus species. Eradication of *B. pertussis* in unimmunized individuals (e.g., neonates) takes longer and requires higher doses than immunized individuals. Oral bioavailability is 38% in adults and children and is not affected by food. Primarily excreted unchanged in the bile, with some hepatic metabolism to inactive metabolites. The prolonged terminal half-life (approximately 80 hours) is thought to be due to extensive uptake and subsequent release of drug from tissues.

**Special Considerations/Preparation**

Oral suspension is available in 300, 600, 900, and 1,200 mg bottles. Reconstitute 300 mg bottle with 9 mL of water to provide a final concentration of 100 mg per 5 mL (20 mg/mL). Shake well before administration. Do not refrigerate. Use within 10 days once bottle has been opened.

Azithromycin for intravenous injection is supplied in single use vials containing 500 mg lyophilized powder. Reconstitute by adding 4.8 mL Sterile Water for Injection, then shake the vial until all the drug is dissolved. The concentration of the reconstituted solution is 100 mg/mL. It is stable at room temperature for 24 hours. **Dilute prior to administration** using a compatible solution to a final concentration of 1 to 2 mg/mL. Diluted solution stable for 24 hours at room temperature or 7 days in refrigerator. Do not use higher concentrations due to local IV site reactions. **Infuse over at least 60 minutes.**

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, NS, 5% Dextrose in 0.45%NaCl with 20 mEq/L KCl, and Lactated Ringer's.

**Terminal Injection Site Compatibility:** Caspofungin.

**Incompatibility:** Amikacin, aztreonam, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, clindamycin, famotidine, fentanyl, furosemide, gentamicin, imipenem-cilastatin, morphine, piperacillin-tazobactam, potassium chloride, ticarcillin-clavulanate, and tobramycin.

### Selected References

- ◆ American Academy of Pediatrics. Pertussis. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 506-507.
- ◆ Centers for Disease Control and Prevention. CDC guidance on shortage of erythromycin (0.5%) ophthalmic ointment-September 2009. Available at: <http://www.cdc.gov/std/treatment/2006/erythromycinointmentshortage.htm>.
- ◆ Centers for Disease Control and Prevention. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis. 2005 CDC guidelines. *MMWR* 2005;54(No. RR-14):pp. 4, 10.
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- ◆ Jacobs RF, Maples HD, Aranda JV, et al. Pharmacokinetics of intravenously administered azithromycin in pediatric patients. *Pediatr Infect Dis J* 2005;24:34-39.
- ◆ Morrison W. Infantile hypertrophic pyloric stenosis in infants treated with azithromycin. *Pediatr Infect Dis J* 2007;26:186-188.
- ◆ Product Information, Pfizer, Inc., 2007.

Dose and Administration, Uses and References updated 10/2009

Dose and Administration, Compatibilities, and References updated 7/2009



**Dose & Administration**

30 mg/kg per dose IV slow push over 5 to 10 minutes, or IM.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Treatment of neonatal sepsis caused by susceptible gram-negative organisms (e.g. *E coli*, *H influenzae*, *Klebsiella*, *Pseudomonas*, and *Serratia*). Generally used in combination with ampicillin (empirical treatment of sepsis) or an aminoglycoside (for synergism against *Pseudomonas* and *Enterobacteriaceae*).

**Monitoring**

Check serum glucose one hour after administration. Measuring serum concentration is not usually necessary. Periodic CBC, AST, ALT.

**Adverse Effects/Precautions**

Aztreonam contains 780 mg L-arginine per gram of drug (23.4 mg/kg body weight per dose). Adequate amounts of glucose must be provided to prevent hypoglycemia. Side effects are rare but include eosinophilia, elevation of serum transaminases, and phlebitis at the injection site.

**Pharmacology**

Aztreonam is a synthetically-produced monocyclic  $\beta$ -lactam antibiotic. Although bactericidal against aerobic gram-negative bacteria, it has virtually no activity against aerobic gram-positive and anaerobic bacteria, thereby producing little alteration of bowel flora. Good tissue and fluid penetration has been demonstrated in adults, along with protein-binding of 50 to 65%. Eliminated renally, primarily as unchanged drug. Serum half-life in neonates is 3 to 9 hours. Aztreonam does not interfere with bilirubin-albumin binding.

*continued...*

**Special Considerations/Preparation**

Available as powder for injection in 1-g, and 2-g vials. Reconstitute 1-g vial with 10 mL of either sterile water for injection or NS (100 mg/mL). **Shake immediately and vigorously.** Reconstituted solution stable for 48 hours at room temperature, 7 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Amikacin, aminophylline, ampicillin, bumetanide, calcium gluconate, caspofungin, cefazolin, cefepime, cefotaxime, ceftiofur, ceftazidime, ceftriaxone, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, enalaprilat, famotidine, fluconazole, furosemide, gentamicin, heparin, hydrocortisone succinate, imipenem, insulin, linezolid, magnesium sulfate, metoclopramide, mezlocillin, morphine, netilmicin, nicardipine, piperacillin, piperacillin/tazobactam, potassium chloride, propofol, quinupristin/dalfopristin, ranitidine, remifentanyl, sodium bicarbonate, ticarcillin/clavulanate, tobramycin, vancomycin, and zidovudine.

**Incompatibility:** Acyclovir, amphotericin B, azithromycin, ganciclovir, lorazepam, metronidazole, and nafcillin.

**Selected References**

- ◆ Uauy R, Mize C, Argyle C, McCracken GH: Metabolic tolerance to arginine: Implications for the safe use of arginine salt-aztreonam combination in the neonatal period. *J Pediatr* 1991;118:965.
- ◆ Cuzzolin L, Fanos V, Zamboni D, et al: Pharmacokinetics and renal tolerance of aztreonam in premature infants. *Antimicrob Agents Chemother* 1991;35:1726.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Likitnukul S, McCracken GH, Threlkeld N, et al: Pharmacokinetics and plasma bactericidal activity of aztreonam in low-birth-weight infants. *Antimicrob Agents Chemother* 1987;31:81.
- ◆ Product Information, Bristol-Myers Squibb, 2007

Compatibilities updated 7/2009

Added 3/1996

**Dose & Administration**

25 mg/m<sup>2</sup> (or approximately 2 mg/kg) per dose every 24 hours, IV infusion via syringe pump over at least 1 hour.

**Uses**

Treatment of patients with refractory Candidemia, intra-abdominal abscesses, peritonitis and pleural space infections, and those patients intolerant of amphotericin B. Treatment of invasive Aspergillosis in patients who are refractory to or intolerant of other therapies.

There are case reports, but not controlled clinical trials, treating endocarditis, osteomyelitis, and meningitis due to *Candida*.

**Monitoring**

Assess IV site for signs of irritation. Periodic measurement of serum potassium, calcium, and hepatic transaminases.

**Adverse Effects/Precautions**

Adverse effects reported in neonates (small number of patients): thrombophlebitis, hypercalcemia, hypokalemia, elevated liver enzymes, and isolated direct hyperbilirubinemia. In pediatric studies, the primary adverse effects were fever, hypokalemia, diarrhea, increased liver enzymes, rash, hypotension and chills.

**Pharmacology**

Caspofungin is the first of a new class of antifungal agents (echinocandins) that inhibit the synthesis of  $\beta$ -(1,3)-D-glucan, an integral component of the fungal cell wall. It is fungicidal against *Candida* species, but fungistatic against *Aspergillus*. The echinocandins are excreted primarily by the liver, presumably metabolized through an O-methyltransferase. They are not metabolized through the CYP enzyme system and therefore have significantly fewer drug-drug interactions than the azoles. Dexamethasone, phenytoin, carbamazepine, nevirapine, and rifampin all induce caspofungin drug clearance, lowering serum concentrations.

**Special Considerations/Preparation**

Cancidas® is supplied as a white to off-white powder cake in single-use vials, containing either 50 or 70 mg. To prepare the 50-mg (5 mg/mL) or 70-mg (7 mg/mL) Cancidas® vial: 1) Equilibrate the refrigerated vial to room temperature. 2) Aseptically add 10.8 mL Normal Saline or Sterile Water for Injection to the vial. The powder cake will dissolve completely with gentle mixing. This reconstituted solution can be stored at room temperature for up to one hour. Visually inspect the reconstituted solution for particulate matter or discoloration. Do not use if the solution is cloudy or has precipitated. Single-use vials: discard remaining unused solution. 3) Remove desired volume of drug based on calculated dose and further dilute in compatible solution (NS, ½ NS, ¼ NS, LR) to a final concentration not to exceed 0.5 mg/mL. The infusion solution can be stored for up to 24 hours at room temperature or up to 48 hours refrigerated. **Do not use diluents containing dextrose.**

continued...

**Solution Compatibility:** NS, 1/2 NS, 1/4 NS, LR.

**Solution Incompatibility:** All solutions containing dextrose.

**Terminal Injection Site Compatibility:** Azithromycin, aztreonam, dobutamine, dopamine, famotidine, fluconazole, insulin, linezolid, meropenem, metronidazole, morphine, potassium chloride, and vancomycin.

**Incompatibility:** Acyclovir, cefazolin, ceftriaxone, clindamycin, furosemide, heparin, and piperacillin/tazobactam.

### Selected References

- ◆ Natale F, Castronovo A, Regoli D, et al: Successful treatment with caspofungin of refractory *Candida krusei* candidemia in a very low birth weight preterm infant. *Pediatr Infect Dis J* 2009;28:452.
- ◆ Saez-Llorens X, Macias M, Maiya P, et al: Pharmacokinetics and safety of caspofungin in neonates and infants less than 3 months of age. *Antimicrob Agents Chemother* 2009;53:869-875.
- ◆ Condie CK, Tyler LS, Baker B, et al: Visual compatibility of caspofungin acetate with commonly used drugs during simulated y-site delivery. *Am J Health-Syst Pharm* 2008;65:454-457, 1597 (errata).
- ◆ Smith PB, Steinbach WJ, Cotton CM, et al: Caspofungin for the treatment of azole resistant candidemia in a premature infant. *J Perinatol* 2007;27:127-129.
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- ◆ Steinbach WJ, Benjamin DK: New agents under development in children and neonates. *Curr Opin Infect Dis* 2005;18:484-489.
- ◆ Pannaraj PS, Walsh TJ, Baker CJ: Advances in antifungal therapy. *Pediatr Infect Dis J* 2005;10:921-923.
- ◆ Walsh TJ, Adamson PC, Seibel NL, et al: Pharmacokinetics, safety, and tolerability of caspofungin in children and adolescents. *Antimicrob Agents Chemother* 2005;49:4536-4545.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al: Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Merck & Co., 2009.

Special Considerations and Compatibility updated 12/2010.

Adverse Effects and References updated 7/2009

Dose updated 03/2009

Added 3/2007

**Dose & Administration**

25 mg/kg per dose IV slow push, or IM.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Use in neonates is generally limited to perioperative infection prophylaxis and treatment of urinary tract and soft tissue infections caused by susceptible organisms, e.g. penicillin-resistant *Staph. aureus*, *Klebsiella*, and *Proteus*.

**Monitoring**

Serum concentrations are not routinely monitored.

**Adverse Effects/Precautions**

Adverse effects are rare, but include phlebitis and eosinophilia.

**Pharmacology**

First generation cephalosporin that is bactericidal against many gram-positive and a few gram-negative organisms. Inactivated by  $\beta$ -lactamase producing organisms. Poor CNS penetration. Renally excreted as unchanged drug. Half-life in neonates is 3 to 5 hours.

**Special Considerations/Preparation**

Available as powder for injection in 500-mg, and 1000-mg vials. Reconstitute 500-mg vial using 2 mL of NS or sterile water for injection to a concentration of 225 mg/mL. Reconstituted solution stable for 24 hours at room temperature or 10 days in refrigerator. A 20 mg/mL dilution may be made by adding 1-mL of reconstituted solution to 10 mL sterile water for injection, or D<sub>5</sub>W.

continued...

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA and fat emulsion. Acyclovir, alprostadil, amikacin, aztreonam, calcium gluconate, clindamycin, enalaprilat, esmolol, famotidine, fluconazole, heparin, insulin, lidocaine, linezolid, magnesium sulfate, midazolam, milrinone, morphine, metronidazole, multivitamins, nicardipine, pancuronium bromide, propofol, prostaglandin E<sub>1</sub>, ranitidine, remifentanyl, and vecuronium.

**Incompatibility:** Amiodarone, caspofungin, cimetidine, and vancomycin.

### Selected References

- ♦ Saez-Llorens X, McCracken GH: Clinical pharmacology of antibacterial agents. In: Remington JS, Klein JO (eds): *Infectious Diseases of the Fetus and Newborn Infant*, ed 5. Philadelphia: WB Saunders Co, 2001.
- ♦ Pickering LK, O'Connor DM, Anderson D, et al: Clinical and pharmacologic evaluation of cefazolin in children. *J Infect Dis* 1973;128:S407.
- ♦ Product Information, Orchid Healthcare, 2006

Compatibilities updated 7/2009

**Dose & Administration**

**Term and preterm infants greater than 28 days of age:** 50 mg/kg per dose every 12 hours.

**Term and preterm infants 28 days of age and younger:** 30 mg/kg per dose every 12 hours.

**Meningitis and severe infections** due to *Pseudomonas aeruginosa* or *Enterobacter* spp.: 50 mg/kg per dose every 12 hours.

Administer via IV infusion by syringe pump over 30 minutes, or IM.

To reduce pain at IM injection site, cefepime may be mixed with 1% lidocaine without epinephrine.

**Uses**

Treatment of serious infections caused by susceptible gram-negative organisms (e.g. *E. coli*, *H. influenzae*, *Enterobacter*, *Klebsiella*, *Morganella*, *Neisseria*, *Serratia*, and *Proteus* species), especially *Pseudomonas aeruginosa* that are resistant to 3<sup>rd</sup> generation cephalosporins. Treatment of serious infections caused by susceptible Gram-positive organisms (e.g. *Strep. pneumoniae*, *Strep. pyogenes*, *Strep. agalactiae*, and *Staph. aureus*).

**Monitoring**

Measuring serum concentration is not usually necessary.

**Adverse Effects/Precautions**

Safety has been documented to be the same as commonly used second- and third-generation cephalosporins. Reported adverse effects are uncommon but include rash, diarrhea, elevated hepatic transaminases, eosinophilia, and positive Coombs' test.

**Pharmacology**

Cefepime is a fourth-generation cephalosporin with treatment efficacy equivalent to third-generation cephalosporins. Potential advantages include: more rapid penetration through the cell wall of Gram-negative pathogens; enhanced stability to hydrolysis by  $\beta$ -lactamases; and enhanced affinity for penicillin-binding proteins. The drug distributes widely in body tissues and fluids (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Protein binding is low ( $\approx$  20%), and it is primarily excreted unchanged in the urine. Serum half-life in infants older than 2 months of age is approximately 2 hours.

**Special Considerations/Preparation**

Available as powder for injection in 500-mg and 1-g, and 2-g vials. Reconstitute 500-mg vial with 5 mL of sterile water for injection to a concentration of 100 mg/mL. Maximum concentration for IV administration is 160 mg/mL, and for IM administration 280 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 7 days refrigerated.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, D<sub>5</sub>LR, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Amikacin, ampicillin, aztreonam, bumetanide, calcium gluconate, clindamycin, dexamethasone, fluconazole, furosemide, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, lorazepam, methylprednisolone, metronidazole, milrinone, piperacillin-tazobactam, potassium chloride, ranitidine, remifentanyl, sodium bicarbonate, ticarcillin/clavulanate, trimethoprim/sulfamethoxazole, and zidovudine.

**Incompatibility:** Acyclovir, aminophylline, amphotericin B, cimetidine, diazepam, dobutamine, dopamine, enalaprilat, erythromycin lactobionate, famotidine, ganciclovir, magnesium sulfate, metoclopramide, midazolam, morphine, nicardipine, phenytoin, tobramycin, and vancomycin.

### Selected References

- ◆ Lima-Rogel V, Medina-Rojas EL, del Carmen Milan-Segovia R, et al: Population pharmacokinetics of cefepime in neonates with severe nosocomial infections. *J Clin Pharm Ther* 2008;33:295-306.
- ◆ Capparelli E, Hochwald C, Rasmussen M, et al: Population pharmacokinetics of cefepime in the neonate. *Antimicrob Agents Chemother* 2005;49:2760-2766.
- ◆ Gutierrez K: Newer antibiotics: cefepime. *NeoReviews* 2004;5:e382-386.
- ◆ Blumer JL, Reed MD, Knupp C: Review of the pharmacokinetics of cefepime in children. *Pediatr Infect Dis J* 2001;20:337-342.
- ◆ Bradley JS, Arrieta A: Empiric use of cefepime in the treatment of lower respiratory tract infections in children. *Pediatr Infect Dis J* 2001;20:343-349.
- ◆ Saez-Llorens XO, O'Ryan M: Cefepime in the empiric treatment of meningitis in children. *Pediatr Infect Dis J* 2001;20:356-361.
- ◆ Kessler RE: Cefepime microbiologic profile and update. *Pediatr Infect Dis J* 2001;20:331-336.
- ◆ Product Information, Bristol-Myers Squibb, 2007.

Compatibilities updated 7/2009

Dose and References updated 1/2009

Added 3/2002



**Dose & Administration**

50 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Disseminated Gonococcal Infections:** 25 mg/kg per dose IV over 30 minutes, or IM every 12 hours for 7 days, with a duration of 10 to 14 days if meningitis is documented.

**Uses**

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E coli*, *H influenzae*, and *Klebsiella*).  
Treatment of disseminated gonococcal infections.

**Monitoring**

Measuring serum concentration is not usually necessary. Periodic CBC.

**Adverse Effects/Precautions**

Side effects are rare but include rash, phlebitis, diarrhea, leukopenia, granulocytopenia, and eosinophilia.

**Pharmacology**

Cefotaxime is one of many third-generation cephalosporin antibiotics. The mechanism of action appears to be by bacterial cell wall disruption. Metabolized in the liver to an active compound, desacetylcefotaxime. The drug distributes widely (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Excreted renally.

Serum half-life in the premature infant is approximately 3 to 6 hours.

continued...

**Special Considerations/Preparation**

Available as powder for injection in 500-mg, 1-g, and 2-g vials. The 500-mg vial is reconstituted with 10 mL sterile water for injection to yield a concentration of 50 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 7 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, alprostadil, amikacin, aztreonam, caffeine citrate, cimetidine, clindamycin, famotidine, gentamicin, heparin, lorazepam, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, oxacillin, penicillin G, potassium chloride, propofol, and remifentanyl.

**Incompatibility:** Azithromycin, fluconazole, protamine sulfate, sodium bicarbonate, and vancomycin.

**Selected References**

- ◆ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010;59(RR-12):1-110.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Kearns GL, Jacobs RF, Thomas BR, et al: Cefotaxime and desacetylcefotaxime pharmacokinetics in very low birth weight neonates. *J Pediatr* 1989;114:461.
- ◆ de Louvois J, Mulhall A, Hurley R: The safety and pharmacokinetics of cefotaxime in the treatment of neonates. *Pediatr Pharmacol* 1982;2:275.
- ◆ Kafetzis DA, Brater DC, Kapiki AN: Treatment of severe neonatal infections with cefotaxime: Efficacy and pharmacokinetics. *J Pediatr* 1982;100:483.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006.

Dose & Administration and References updated 12/2010  
Compatibilities updated 7/2009

**Dose & Administration**

25 to 33 mg/kg per dose IV infusion by syringe pump over 30 minutes.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Use in neonates is generally limited to treatment of skin, intra-abdominal and urinary tract infections caused by susceptible bacteria - anaerobes (e.g. *Bacteroides fragilis*), gram positives (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, and other streptococci except enterococcus) and gram negatives (e.g. *Haemophilus influenzae*, *Klebsiella* sp., *E. coli*, *Proteus vulgaris*, and *Neisseria gonorrhoeae*).

**Monitoring**

Serum concentrations are not routinely monitored.

**Adverse Effects/Precautions**

Adverse effects are rare. Transient eosinophilia and elevation of hepatic transaminases have been reported in less than 3% of treated patients. Severe overdose can cause tachypnea, pallor, hypotonia, and metabolic acidosis.

**Pharmacology**

Broad spectrum bactericidal second generation cephalosporin that has enhanced activity against anaerobic bacteria. Inhibits bacterial cell wall synthesis by binding to one or more penicillin-binding proteins. Not inactivated by  $\beta$ -lactamase. Poor CNS penetration. Highly protein bound. Renally excreted as unchanged drug (85% to 90%). Half-life in term neonates is approximately 1.4 hours, and 2.3 hours in preterm neonates —considerably longer than children (0.6 hours) and adults (0.8 hours).

continued...

**Special Considerations/Preparation**

Available as powder for injection in 1-g. and 2-g vials.

**IV administration:** Reconstitute 1-g vial with 9.5 mL sterile water for injection to a concentration of 100 mg/mL. A 40 mg/mL dilution may be made by adding 4 mL of reconstituted solution to 6 mL sterile water for injection, or D<sub>5</sub>W. Stable for 18 hours at room temperature or 7 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA and fat emulsion. Acyclovir, amikacin, aztreonam, cimetidine, clindamycin, dopamine, famotidine, fluconazole, gentamicin, heparin, insulin, lidocaine, linezolid, magnesium sulfate, metronidazole, morphine, multivitamins, oxacillin, penicillin G, potassium chloride, propofol, ranitidine, remifentanyl, sodium bicarbonate, and tobramycin.

**Incompatibility:** Erythromycin lactobionate, sodium bicarbonate, and vancomycin.

**Selected References**

- ◆ Regazzi MB, Chirico G, Cristiani D, et al: Cefoxitin in newborn infants. *Eur J Clin Pharmacol* 1983;25:507-509.
- ◆ Yogeve R, Delaplane D, Wiringa K: Cefoxitin in a neonate. *Ped Infect Dis J* 1983;2:342-343.
- ◆ Farmer K: Use of cefoxitin in the newborn. *New Zealand Med J* 1982;95:398.
- ◆ Marget W: Tenfold overdose of cefoxitin in a newborn. *Infection* 1982;10:243.
- ◆ Brogden RN, Heel RC, Speight TM, et al: Cefoxitin: A review of its antibacterial activity, pharmacological properties and therapeutic use. *Drugs* 1979;17:1-37.
- ◆ Feldman WE, Moffitt S, Sprow N: Clinical and pharmacokinetic evaluation of parenteral cefoxitin in infants and children. *Antimicrob Agents Chemother* 1980;17:669-674.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006.

Compatibilities updated 7/2009

Text updated 3/2008

**Dose & Administration**

30 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM. To reduce pain at IM injection site, ceftazidime may be mixed with 1% lidocaine without epinephrine.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	8

**Uses**

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E coli*, *H influenzae*, *Neisseria*, *Klebsiella*, and *Proteus* species), especially *Pseudomonas aeruginosa*. Resistance among strains of *Serratia* and *Enterobacteriaceae* is increasing.

**Monitoring**

Measuring serum concentration is not usually necessary.

**Adverse Effects/Precautions**

<sup>1</sup> Reported adverse effects are uncommon but include rash, diarrhea, elevated hepatic transaminases, eosinophilia, and positive Coombs' test.

**Pharmacology**

Ceftazidime is one of many third-generation cephalosporins. The drug distributes widely in body tissues and fluids (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Protein binding is low, and it is excreted unchanged in the urine. Ceftazidime is synergistic with aminoglycosides. Serum half-life in neonates is 3 to 12 hours.

continued...

**Special Considerations/Preparation**

Available as powder for injection in 500-mg and 1-g, 2-g, and 6-g vials.

**Intravenous solution:** Reconstitute 500-mg vial with 10 mL of sterile water for injection to make a concentration of 50 mg/mL. Reconstituted solution stable for 12 hours at room temperature, 3 days refrigerated.

**Intramuscular solution:** Prepared by reconstituting 500-mg vial with 2.2 mL of 1% lidocaine without epinephrine or Sterile Water to a concentration of 200 mg/mL. Solution is stable for 12 hours at room temperature, 3 days refrigerated.

All dosage forms approved for pediatric use contain sodium carbonate; when reconstituted, carbon dioxide bubbles will form. Using a vented needle may help reduce spraying and leaking.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, aminophylline, aztreonam, cimetidine, clindamycin, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, famotidine, furosemide, gentamicin, heparin, ibuprofen lysine, linezolid, metronidazole, milrinone, morphine, potassium chloride, propofol, ranitidine, remifentanyl, sodium bicarbonate, tobramycin, and zidovudine.

**Incompatibility:** Amiodarone, azithromycin, erythromycin lactobionate, fluconazole, midazolam, nicardipine, phenytoin, and vancomycin.

**Selected References**

- ◆ Prober CC, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Tessin I, Thiringer K, Trollfors B, Brorson JE: Comparison of serum concentrations of ceftazidime and tobramycin in newborn infants. *Eur J Pediatr* 1988;147:405.
- ◆ Odio CM, Umana MA, Saenz A, et al: Comparative efficacy of ceftazidime vs. carbenicillin and amikacin for treatment of neonatal septicemia. *Pediatr Infect Dis* 1987;6:371.
- ◆ McCracken GH, Threlkeld N, Thomas ML: Pharmacokinetics of ceftazidime in newborn infants. *Antimicrob Agents Chemother* 1984;26:583.
- ◆ Product Information, GlaxoSmithKline, 2007.

Compatibilities updated 10/2009

**Dose & Administration**

**Sepsis:** 50 mg/kg every 24 hours.

**Meningitis:** 100 mg/kg loading dose, then 80 mg/kg every 24 hours.

**Gonococcal Infections:**

**Disseminated Gonococcal Infections:** 25 to 50 mg/kg/day IV/IM in a single daily dose for 7 days, with a duration of 10 to 14 days if meningitis is documented.

**Gonococcal Infection, Prophylaxis:** 25 to 50 mg/kg (maximum 125 mg) IV/IM as a single dose.

**Uncomplicated Gonococcal Ophthalmia:** 25 to 50 mg/kg (maximum 125 mg) IV/IM as a single dose. (Note: topical antibiotic therapy alone is inadequate and is unnecessary if systemic treatment is administered.)

**IV administration:** Infusion by syringe pump over 30 minutes. Avoid administration of calcium-containing solutions or products within 48 hours of the last administration of ceftriaxone.

**IM administration:** To reduce pain at the injection site, reconstitute with 1% lidocaine without epinephrine.

**Uses**

Treatment of neonatal sepsis and meningitis caused by susceptible gram-negative organisms (e.g. *E coli*, *Pseudomonas*, *Klebsiella*, *H influenzae*). Treatment of gonococcal infections.

**Monitoring**

CBC for eosinophilia, thrombocytosis, leukopenia. Serum electrolytes, BUN, creatinine. AST, ALT, bilirubin. Consider abdominal ultrasonography.

**Adverse Effects/Precautions**

**Not recommended for use in neonates with hyperbilirubinemia.** Displaces bilirubin from albumin binding sites, resulting in higher free bilirubin serum concentrations. **Concurrent administration of ceftriaxone and calcium-containing solutions or products in neonates is contraindicated.** There have been 7 reported cases of cardiorespiratory arrest in young infants, with 6 deaths, associated with concurrent administration of ceftriaxone and calcium-containing intravenous solutions. In all cases, the ceftriaxone dose (150 to 200 mg/kg/day) significantly exceeded the FDA recommended dose and/or was administered IV push. Crystalline material or white precipitate was noted in vascular beds on autopsy (primarily in the lungs) in 4 of the 5 infants for which results were available. Eosinophilia, thrombocytosis, leukopenia. Increase in bleeding time. Diarrhea. Increase in BUN and serum creatinine. Increase in AST and ALT. Skin rash. Transient gallbladder precipitations occasionally associated with colicky abdominal pain, nausea, and vomiting.

**Pharmacology**

Ceftriaxone is one of many third-generation cephalosporin antibiotics. The drug distributes widely (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). It is eliminated unchanged by both biliary (40%) and renal mechanisms. Serum half-life in premature infants is 5 to 16 hours. Dosage adjustment is necessary only for patients with combined hepatic and renal failure.

*continued...*

**Special Considerations/Preparation**

**Intravenous solution:** Available as a powder for injection in 250-mg, 500-mg, 1-g, and 2-g vials. Prepared by reconstituting powder with compatible solution (sterile water for injection, D<sub>5</sub>W, or D<sub>10</sub>W) to a concentration of 100 mg/mL. Reconstituted solution is stable for 2 days at room temperature, 10 days refrigerated. A dark color may appear after reconstitution; however, potency is retained. To make 40-mg/mL solution add 6.2 mL to the 250-mg vial.

**Intramuscular solution:** Prepared by reconstituting 250-mg vial with 0.9 mL of 1% lidocaine without epinephrine to a concentration of 250 mg/mL. Solution is stable for 24 hours at room temperature, 3 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Solution Incompatibility:** Any calcium-containing solution.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, amiodarone, aztreonam, clindamycin, famotidine, gentamicin, heparin, linezolid, metronidazole, morphine, potassium chloride, propofol, remifentanyl, sodium bicarbonate, and zidovudine.

**Incompatibility:** Aminophylline, azithromycin, calcium chloride, calcium gluconate, caspofungin, fluconazole and vancomycin.

**Selected References**

- ◆ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. MMWR 2010;59(RR-12):1-110.
- ◆ Bradley JS, Wassel RT, Lee L, Nambiar S: Intravenous ceftriaxone and calcium in the neonate: Assessing the risk for cardiopulmonary adverse events. Pediatrics 2009;123:e609-e613.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. Pediatr Infect Dis J 1990;9:111.
- ◆ Schaad UB, Suter S, Gianella-Borradori A, et al: A comparison of ceftriaxone and cefuroxime for the treatment of bacterial meningitis in children. N Engl J Med 1990;332:141.
- ◆ Fink S, Karp W, Robertson A: Ceftriaxone effect on bilirubin-albumin binding. Pediatrics 1987;80:873.
- ◆ Laga M, Naamara W, Brunham RC, et al: Single-dose therapy of gonococcal ophthalmia neonatorum with ceftriaxone. N Engl J Med 1986;315:1382.
- ◆ Yogev R, Shulman ST, Chadwick E, et al: Once daily ceftriaxone for central nervous system infections and other serious pediatric infections. Pediatr Infect Dis J 1986;5:298.
- ◆ Martin E, Koup JR, Paravicini U, Stoeckel K: Pharmacokinetics of ceftriaxone in neonates and infants with meningitis. J Pediatr 1984;105:475.
- ◆ Schaad UB, Stoeckel K: Single-dose pharmacokinetics of ceftriaxone in infants and young children. Antimicrob Agents Chemother 1982;21:248.
- ◆ Product Information, Roche, 2009.

Dose & Administration and References updated 12/2010

Compatibilities updated 7/2009

Adverse Effects updated 4/2009



**Dose & Administration**

**Loading dose:** 20 mg/kg IV infusion by syringe pump over 30 minutes.

**Maintenance dose:** (Begin 12 hours after loading dose.)

Premature infants under 1 month of age: 2.5 mg/kg per dose every 6 hours.

Fullterm infants under 1 week of age and premature infants over 1 month of age: 5 mg/kg per dose every 6 hours.

Fullterm infants over 1 week of age: 12.5 mg/kg per dose every 6 hours.

(Absorption of oral chloramphenicol palmitate is erratic in newborns.)

**Uses**

A wide-spectrum antimicrobial bacteriostatic agent. May be bactericidal to species such as *H influenzae* and *Neisseria meningitidis*.

**Monitoring**

Close monitoring of serum concentration is mandatory. Small changes in dose and interval can lead to disproportionately large changes in serum concentration. Therapeutic peak serum concentration: 10 to 25 mcg/mL. Monitor CBC and reticulocyte counts. Assess hepatic and renal function.

**Adverse Effects/Precautions**

Reversible bone marrow suppression, irreversible aplastic anemia. Serum concentration greater than 50 mcg/mL has been associated with the "gray baby" syndrome (ie, abdominal distention, pallid cyanosis, vasomotor collapse; may lead to death within hours of onset). Fungal overgrowth.

**Black Box Warning**

According to the manufacturer's black box warning, serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia) are known to occur. There have been reports of aplastic anemia which later terminated in leukemia. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. It is essential that adequate blood studies be made during treatment.

**Pharmacology**

Both esters (succinate and palmitate) are biologically inactive prodrugs. Hydrolysis to the active compound is erratic in newborns. Metabolized by hepatic glucuronyl transferase. Hepatically and renally eliminated. Inhibits metabolism of phenobarbital, phenytoin, and other agents.

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**Special Considerations/Preparation**

Chloramphenicol succinate is available as powder for injection in a 1-g vial. Reconstitute with 10 mL sterile water for injection, or D<sub>5</sub>W to a concentration of 100 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, ampicillin, calcium chloride, calcium gluconate, dopamine, enalaprilat, esmolol, heparin, hydrocortisone succinate, lidocaine, magnesium sulfate, metronidazole, morphine, nafcillin, nicardipine, oxacillin, penicillin G, pentobarbital, potassium chloride, ranitidine, sodium bicarbonate, and vitamin K<sub>1</sub>.

**Incompatibility:** Erythromycin lactobionate, fluconazole, metoclopramide, phenytoin, and vancomycin.

**Selected References**

- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 70.
- ◆ Rajchgot P, Prober CG, Soldin S: Initiation of chloramphenicol therapy in the newborn infant. *J Pediatr* 1982;101:1018.
- ◆ Glazer JP, Danish MA, Plotkin SA, Yaffe SJ: Disposition of chloramphenicol in low birth weight infants. *Pediatrics* 1980;66:573.
- ◆ Product Information, Abraxis, 2006.

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

**Dose & Administration**

5 to 7.5 mg/kg per dose IV infusion by syringe pump over 30 minutes, or orally

Increase dosing interval in patients with significant liver dysfunction.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Bacteriostatic antibiotic used for the treatment of bacteremia and pulmonary and deep tissue infections caused by anaerobic bacteria and some gram-positive cocci. Clindamycin should not be used in the treatment of meningitis.

**Monitoring**

Assess liver function. Monitor GI status closely. Therapeutic serum concentration ranges from 2 to 10 mcg/mL (bioassay yields variable results).

**Adverse Effects/Precautions****Black Box Warning**

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clindamycin, and may range in severity from mild to life-threatening. Because clindamycin therapy has been associated with severe colitis which may end fatally, it should be reserved for serious infections where less toxic antimicrobial agents are inappropriate. Diarrhea, colitis, and pseudomembranous colitis have been observed to begin up to several weeks following cessation of therapy with clindamycin. Hypersensitivity reactions, jaundice, and liver function test abnormalities have been reported in association with clindamycin therapy.

**Pharmacology**

Clindamycin inhibits bacterial protein synthesis and is primarily bacteriostatic at therapeutically attainable concentrations. Widely distributed into most tissues, especially the lung. Poor CSF penetration. Oral clindamycin is completely absorbed from the GI tract. Highly protein bound. Almost complete metabolism in the liver, with excretion via bile and feces. Available data in neonates suggest extremely variable clearance, especially in premature infants. No data are available regarding conversion of ester to active drug.

*continued...*

**Special Considerations/Preparation**

Oral preparation (clindamycin palmitate) is reconstituted with sterile water for injection, yielding a 75 mg per 5 mL solution.

**Do not refrigerate.** Stable at room temperature for 2 weeks.

IV preparation (clindamycin phosphate) is available as a 150 mg/mL solution in 2-mL, 4-mL, and 6-mL vials containing 9.45 mg/mL benzyl alcohol. It should be diluted using D<sub>5</sub>W, NS, or LR to a maximum concentration of 18 mg/mL, and infused at a rate no greater than 30 mg/min. Also available in premixed bags (50 mL) without benzyl alcohol containing 300 mg, 600 mg or 900 mg of clindamycin.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, amikacin, amiodarone, ampicillin, aztreonam, caffeine citrate, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, cimetidine, enalaprilat, esmolol, gentamicin, heparin, hydrocortisone succinate, linezolid, magnesium sulfate, metoclopramide, metronidazole, midazolam, milrinone, morphine, netilmicin, nicardipine, penicillin G, piperacillin, piperacillin/tazobactam, potassium chloride, propofol, prostaglandin E<sub>1</sub>, ranitidine, remifentanyl, sodium bicarbonate, tobramycin, and zidovudine.

**Incompatibility:** Aminophylline, azithromycin, barbiturates, caspofungin, fluconazole, and phenytoin.

**Selected References**

- ◆ Koren G, Zarfin Y, Maresky D, et al: Pharmacokinetics of intravenous clindamycin in newborn infants. *Pediatr Pharmacol* 1986;5:287.
- ◆ Bell MJ, Shackelford P, Smith R, Schroeder K: Pharmacokinetics of clindamycin phosphate in the first year of life. *J Pediatr* 1984;105:482.
- ◆ Feigin RD, Pickering LK, Anderson D, et al: Clindamycin treatment of osteomyelitis and septic arthritis in children. *Pediatrics* 1975;55:213.
- ◆ Lwin N, Collipp PJ: Absorption and tolerance of clindamycin 2-palmitate in infants below 6 months of age. *Curr Ther Res Clin Exp* 1970;12:648.
- ◆ Product Information, Pfizer, 2007.

Adverse Effects/Precautions and References updated 12/2010

Compatibilities updated 7/2009

Special Considerations updated 3/2008

**Dose & Administration**

**Treatment of pneumonitis and conjunctivitis due to *Chlamydia trachomatis*:** 12.5 mg/kg per dose orally every 6 hours for 14 days.

**Other infections and prophylaxis:** 10 mg/kg per dose orally every 6 hours.

Oral treatment with E. ethylsuccinate (e.g., E. E. S.<sup>®</sup>, EryPed<sup>®</sup>).

**Treatment and prophylaxis of pertussis:** 12.5 mg/kg per dose orally every 6 hours for 14 days. The drug of choice in infants younger than 1 month of age is azithromycin. Administer with infant formula to enhance absorption of the ethylsuccinate and reduce possible GI side effects.

**Severe infections when oral route unavailable:** 5 to 10 mg/kg per dose IV infusion by syringe pump over at least 60 minutes every 6 hours.

**Do not administer IM.**

**Prophylaxis of ophthalmia neonatorum:** Ribbon of 0.5% ointment instilled in each conjunctival sac.

**Treatment of feeding intolerance due to dysmotility:** 10 mg/kg per dose orally every 6 hours for 2 days, followed by 4 mg/kg per dose orally every 6 hours for 5 days.

**Uses**

Treatment of infections caused by *Chlamydia*, *Mycoplasma*, and *Ureaplasma*. Treatment for and prophylaxis against *Bordetella pertussis*. As a substitute for penicillin in situations of significant allergic intolerance. As a prokinetic agent in cases of feeding intolerance.

**Monitoring**

Watch for diarrhea and signs of abdominal discomfort. CBC for eosinophilia. **Monitor heart rate and blood pressure closely during IV administration.** Observe IV site for signs of infiltration.

**Adverse Effects/Precautions**

The risk of hypertrophic pyloric stenosis is increased 10-fold in neonates under 2 weeks of age who receive oral erythromycin for pertussis prophylaxis (1 additional case per every 42 infants treated). No studies of premature infants with feeding intolerance have been large enough to assess safety. Two reported cases of severe bradycardia and hypotension occurring during IV administration of erythromycin lactobionate. Intrahepatic cholestasis. Loose stools occur infrequently. Bilateral sensorineural hearing loss has been reported rarely in adults, usually associated with intravenous administration and renal or hepatic dysfunction. The hearing loss occurred after the first few doses and was reversible after discontinuing the drug. Venous irritation is common when using the IV dosage form.

*continued...*

**Pharmacology**

Erythromycin may be bacteriostatic or bactericidal depending on the tissue concentration of drug and the microorganism involved. IV administration of E. lactobionate to preterm infants, using doses of 6.25 to 10 mg/kg, yielded peak serum concentrations of 1.9 to 3.7 mcg/mL and a half-life of 2 hours. The drug penetrates poorly into the CNS, is concentrated in the liver and bile, and is excreted via the bowel. It is a motilin receptor agonist and induces stomach and small intestine motor activity. Plasma clearance of midazolam is reduced by 50%. Digoxin, midazolam, theophylline and carbamazepine serum concentrations may be significantly increased because of prolongation of their half-life.

**Special Considerations/Preparation**

Erythromycin ethylsuccinate oral suspension is available in concentrations of 200 mg- and 400 mg per 5 mL. Refrigeration not required except to preserve taste. Shake suspension well before administering. To prepare a 20 mg/mL dilution of the oral suspension, dilute 5 mL of the 200 mg/5 mL (40 mg/mL) erythromycin ethylsuccinate suspension (suspension made from powder for suspension only) up to a final volume of 10 mL with sterile water. Erythromycin ethylsuccinate suspension made from powder for suspension, at usual concentrations of 40 mg/mL and 80 mg/mL, is stable for 35 days at room temperature.

Available as powder for injection in 500-mg and 1-g vials. Reconstitute 500-mg vial with 10 mL of sterile water for injection to concentration of 50 mg/mL. Reconstituted solution stable for 24 hours at room temperature or 2 weeks in refrigerator. After reconstitution, dilute to a concentration of 1 to 5 mg/mL for infusion. To make a 5-mg/mL dilution, add 1 mL of reconstituted solution to 9 mL sterile water for injection. Use diluted drug within 8 hours.

Erythromycin ophthalmic is available as a 0.5% ointment. In the event of a shortage, the CDC recommends azithromycin ophthalmic solution 1%. Tobramycin ophthalmic ointment may be used if azithromycin solution is not available.

**Solution Compatibility:** NS and sterile water for injection.

**Solution Incompatibility:** D<sub>5</sub>W and D<sub>10</sub>W (unless buffered with 4% sodium bicarbonate to maintain stability).

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, amiodarone, cimetidine, enalaprilat, esmolol, famotidine, heparin, hydrocortisone succinate, lidocaine, lorazepam, magnesium sulfate, midazolam, morphine, nifedipine, penicillin G, pentobarbital, potassium chloride, ranitidine, sodium bicarbonate, and zidovudine.

**Incompatibility:** Ampicillin, cefepime, cefotaxime, ceftazidime, chloramphenicol, fluconazole, furosemide, linezolid, and metoclopramide.

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References updated 12/2010

Special Considerations updated 10/2009

Compatibilities updated 7/2009





**Dose & Administration**

**Invasive Candidiasis:** 12 to 25 mg/kg loading dose, then 6 to 12 mg/kg per dose IV infusion by syringe pump over 30 minutes, or orally.

Consider the higher doses for treating severe infections or *Candida* strains with higher MICs (4 to 8 mcg/mL). Extended dosing intervals should be considered for neonates with renal insufficiency (serum creatinine greater than 1.3 mg/dL).

Note: The higher doses are based on recent pharmacokinetic data but have not been prospectively tested for efficacy or safety.

**Prophylaxis:** 3 mg/kg per dose via IV infusion twice weekly, or orally. A dose of 6 mg/kg twice weekly may be considered if targeting *Candida* strains with higher MICs (4 to 8 mcg/mL). Consider prophylaxis only in VLBW infants at high risk for invasive fungal disease.

**Thrush:** 6 mg/kg on Day 1, then 3 mg/kg per dose every 24 hours orally.

To use the dosing chart, please refer to explanatory note on page 1.

**Invasive Candidiasis Dosing Interval Chart**

Gest. Age (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 14	48
	>14	24
30 and older	0 to 7	48
	>7	24

**Uses**

Treatment of systemic infections, meningitis, and severe superficial mycoses caused by *Candida* species. Resistance has been reported with *C. glabrata* and *C. krusei* and in patients receiving long-term suppressive therapy.

**Monitoring**

Serum fluconazole concentrations are not routinely followed. Assess renal function. Follow AST, ALT, and direct bilirubin, especially in patients on the higher doses. Periodic CBC for eosinophilia.

**Adverse Effects/Precautions**

Data in neonates are limited. Reversible elevations of transaminases have occurred in 12% of children. A retrospective study using historical controls reports direct hyperbilirubinemia in the absence of elevated transaminases in some infants treated prophylactically for 6 weeks. Interferes with metabolism of barbiturates and phenytoin. May also interfere with metabolism of aminophylline, caffeine, theophylline, and midazolam.

**Contraindicated** in patients receiving **cisapride** due to precipitation of life-threatening arrhythmias.

*continued...*

**Pharmacology**

Water-soluble triazole antifungal agent. Inhibits cytochrome P-450-dependent ergosterol synthesis. Well absorbed after oral administration, with peak serum concentrations reached within 1 to 2 hours. Less than 12% protein binding. Good penetration into CSF after both oral and IV administration. Serum half-life is 30 to 180 hours in severely ill VLBW infants in the first 2 weeks of life and approximately 17 hours in children. Primarily excreted unchanged in the urine.

**Special Considerations/Preparation**

Available as a premixed solution for IV injection in concentrations of 200 mg/100 mL and 400 mg/200 mL in Viaflex® bags or glass bottles (2 mg/mL). Do not remove overwrap from Viaflex® bag until ready for use. **Store at room temperature. Do not freeze.**

Oral dosage form is available as a powder for suspension in concentrations of 10 mg/mL and 40 mg/mL. Prepare both concentrations by adding 24 mL distilled water to bottle of powder and shaking vigorously. Each bottle will deliver 35 mL of suspension. Suspension is stable at room temperature for 2 weeks. **Do not freeze.**

**Solution Compatibility:** D<sub>5</sub>W and D<sub>10</sub>W.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, aminophylline, amiodarone, aztreonam, caspofungin, cefazolin, cefepime, ceftazidime, cimetidine, dexamethasone, dobutamine, dopamine, famotidine, ganciclovir, gentamicin, heparin, hydrocortisone succinate, intravenous immune globulin (human), linezolid, lorazepam, meropenem, metoclopramide, metronidazole, midazolam, morphine, nafcillin, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenytoin, piperacillin/tazobactam, potassium chloride, propofol, quinupristin/dalfopristin, ranitidine, remifentanyl, ticarcillin/clavulanate, tobramycin, vancomycin, vecuronium, and zidovudine.

**Incompatibility:** Amphotericin B, ampicillin, calcium gluconate, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, clindamycin, digoxin, erythromycin lactobionate, furosemide, imipenem, piperacillin, ticarcillin, and trimethoprim-sulfamethoxazole.

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Special Considerations and References updated 12/2010

Dose & Administration and Monitoring updated 1/2010

Compatibilities updated 7/2009



**Dose & Administration**

12.5 to 37.5 mg/kg per dose every 6 hours orally. Increase dosing interval if renal dysfunction is present.

**Uses**

Antifungal agent used in combination with amphotericin B or fluconazole for treatment of infections caused by *Candida*, *Cryptococcus*, and other sensitive fungi.

**Monitoring**

Desired peak serum concentration ranges from 50 to 80 mcg/mL. Assess renal function. Follow GI status closely. Twice-weekly CBC and platelet counts. Periodic AST, ALT.

**Adverse Effects/Precautions**

Toxicities are related to serum concentration above 100 mcg/mL, and are usually reversible if the drug is stopped or the dose is reduced. Fatal bone marrow depression (related to fluorouracil production), hepatitis, severe diarrhea, rash. Amphotericin B may increase toxicity by decreasing renal excretion.

**Black Box Warning**

According to the manufacturer's black box warning, extreme caution is recommended in patients with impaired renal function. Close monitoring of hematologic, renal, and hepatic status of all patients is essential.

**Pharmacology**

Well absorbed orally. Transformed within cell to fluorouracil, which interferes with RNA synthesis. Excellent penetration into CSF and body tissues. 90% renal elimination of unchanged drug, proportional to GFR. Serum half-life in adults is 3 to 5 hours if renal function is normal, but 30 to 250 hours if renal impairment is present. Limited pharmacokinetic data in premature infants. Resistance develops frequently if used alone. Synergistic with amphotericin even if treating resistant strain.

**Special Considerations/Preparation**

Flucytosine is available only in 250 and 500-mg capsules. A pediatric suspension (10 mg/mL) may be prepared using distilled water; adjust pH from 5 to 7 with dilute sodium hydroxide. The capsule contains talc, which forms large-particle precipitates of inactive compound. The remaining suspension, containing the active drug, may be decanted. Shake well before use. The suspension is stable for 7 days at room temperature.

*continued...*

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Adverse Effects/Precautions updated 1/2009

**Dose & Administration**

6 mg/kg per dose every 12 hours IV infusion by syringe pump over 1 hour. Treat for a minimum of 6 weeks if possible. Reduce the dose by half for significant neutropenia (less than 500 cells/mm<sup>3</sup>).

**Chronic oral suppression:** 30 to 40 mg/kg per dose every 8 hours orally.

**Uses**

Prevention of progressive hearing loss and lessening of developmental delays in babies with symptomatic congenital CMV infection involving the central nervous system.

**Monitoring**

CBC every 2 to 3 days during first 3 weeks of therapy, weekly thereafter if stable.

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, the clinical toxicity of ganciclovir includes granulocytopenia, anemia, and thrombocytopenia.

Significant neutropenia will occur in the majority of treated patients. Discontinue treatment if the neutropenia does not resolve after reducing the dosage by half.

**Pharmacology**

Ganciclovir is an acyclic nucleoside analog of guanine that inhibits replication of herpes viruses in vivo. There is large interpatient variability in pharmacokinetic parameters. Mean half-life in infants less than 49 days postnatal age is 2.4 hours. Metabolism is minimal; almost all drug is excreted unchanged in the urine via glomerular filtration and active tubular secretion.

**Special Considerations/Preparation**

Cytovene® is supplied as lyophilized powder for injection, 500 mg per vial. Reconstitute by injecting 10 mL of sterile water for injection into the vial. Do not use bacteriostatic water for injection containing parabens; it is incompatible with ganciclovir and may cause precipitation. Shake the vial to dissolve the drug. Visually inspect the reconstituted solution for particulate matter and discoloration prior to proceeding with infusion solution. Discard the vial if particulate matter or discoloration is observed.

Reconstituted solution in the vial is stable at room temperature for 12 hours. **Do not refrigerate**, may cause precipitation. The pH is approximately 11; use caution when handling. Osmolarity is 320 mOsm/kg.

Based on patient weight, remove the appropriate volume of the reconstituted solution (ganciclovir concentration 50 mg/mL) from the vial and add to a compatible diluent fluid to make a final infusion concentration less than 10 mg/mL. Although stable for 14 days, the infusion solution must be used within 24 hours of dilution to reduce the risk of bacterial contamination. Refrigerate the infusion solution. **Do not freeze.**

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Available as 250-mg and 500-mg capsules. Prepare oral suspension in a vertical-flow laminar hood. Oral suspension (100 mg/mL) may be prepared by emptying eighty (80) 250-mg capsules into a glass mortar wetted and triturated with Oral-Sweet® to a smooth paste. Add 50-mL of Oral-Sweet® to the paste, mix, and transfer contents to an amber polyethylene terephthalate bottle. Rinse the mortar with another 50 mL of Oral-Sweet® and transfer contents to the bottle. Add enough Oral-Sweet® to make a final volume of 200 mL. Stable for 123 days when stored at 23 to 25 degrees C. **Protect from light.**

**Solution Compatibility:** NS, D<sub>5</sub>W, and LR.

**Solution Incompatibility:** Dex/AA.

**Terminal Injection Site Compatibility:** Enalaprilat, fluconazole, linezolid, propofol, and remifentanyl.

**Incompatibility:** Fat emulsion. Aztreonam, cefepime, and piperacillin/tazobactam.

### Selected References

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Special Considerations updated 12/2010

Uses and References updated 2/2010

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009



**Dose & Administration**

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Chart**

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
≤29*	0 to 7	5	48
	8 to 28	4	36
	≥29	4	24
30 to 34	0 to 7	4.5	36
	≥8	4	24
≥35	ALL	4	24
* or significant asphyxia, PDA, or treatment with indomethacin			

**Uses**

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a  $\beta$ -lactam antibiotic.

**Monitoring**

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible. Therapeutic serum concentrations: **Peak:** 5 to 12 mcg/mL (or  $C_{max}/MIC$  ratio greater than 8:1) **Trough:** 0.5 to 1 mcg/mL.

**Suggested Dosing Intervals**

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤1	≈ 8	24
1.1 to 2.3	≈ 12	36
2.4 to 3.2	≈ 15	48
≥3.3		Measure level in 24 hours

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**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia. The use of gentamicin ointment for newborn ocular prophylaxis has been associated with periocular ulcerative dermatitis.

**Pharmacology**

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a  $\beta$ -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of gentamicin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

**Special Considerations/Preparation**

Pediatric injectable solution available in a concentration of 10 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions and fat emulsion. Acyclovir, alprostadil, amiodarone, aztreonam, caffeine citrate, cefepime, cefotaxime, ceftazidime, ceftriaxone, cimetidine, clindamycin, dopamine, enalaprilat, esmolol, famotidine, fluconazole, gentamicin, heparin (concentrations of 1 unit/mL or less), insulin, linezolid, lorazepam, magnesium sulfate, meropenem, metronidazole, midazolam, milrinone, morphine, nicardipine, pancuronium bromide, penicillin G, prostaglandin E<sub>1</sub>, ranitidine, remifentanyl, vecuronium, and zidovudine.

**Incompatibility:** Amphotericin B, ampicillin, azithromycin, furosemide, imipenem/cilastatin, heparin (concentrations greater than 1 unit/mL), indomethacin, mezlocillin, nafcillin, oxacillin, propofol, and ticarcillin/clavulanate.

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- ◆ Williams BS, Ransom JL, Gal P, et al: Gentamicin pharmacokinetics in neonates with patent ductus arteriosus. *Crit Care Med* 1997;25:273-75.
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Adverse Effects/Precautions and References updated 7/2010

Compatibilities updated 7/2009

Text, Compatibilities, and References updated 3/2007



**Dose & Administration**

20 to 25 mg/kg per dose every 12 hours IV infusion over 30 minutes.

**Uses**

Restricted to treatment of non-CNS infections caused by bacteria, primarily Enterobacteriaceae and anaerobes, resistant to other antibiotics.

**Monitoring**

Periodic CBC and hepatic transaminases. Assess IV site for signs of phlebitis.

**Adverse Effects/Precautions**

Seizures occur frequently in patients with meningitis, preexisting CNS pathology, and severe renal dysfunction. Local reactions at the injection site and increased platelet counts are the most frequent adverse effects. Others including eosinophilia, elevated hepatic transaminases, and diarrhea also occur in more than 5% of patients.

**Pharmacology**

Imipenem is a broad-spectrum carbapenem antibiotic combined in a 1:1 ratio with cilastatin, a renal dipeptidase inhibitor with no intrinsic antibacterial activity. Bactericidal activity is due to inhibition of cell wall synthesis. Clearance is directly related to renal function. Serum half-life of imipenem in neonates is 2.5 hours; the half-life of cilastatin is 9 hours.

**Special Considerations/Preparation**

Available as powder for injection in 250-mg, and 500-mg vials. Reconstitute with 10 mL of compatible diluent. When reconstituted with compatible diluent, solution is stable for 4 hours at room temperature, 24 hours refrigerated. Maximum concentration for infusion is 5 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Acyclovir, aztreonam, cefepime, famotidine, insulin, linezolid, midazolam, propofol, remifentanyl, and zidovudine.

**Incompatibility:** Amikacin, amiodarone, azithromycin, fluconazole, gentamicin, lorazepam, milrinone, sodium bicarbonate, and tobramycin.

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- ◆ Nalin DR, Jacobsen CA: Imipenem/cilastatin therapy for serious infections in neonates and infants. *Scand J Infect Dis* 1987;Suppl.2:46.
- ◆ Product Information, Merck, 2006

Compatibilities updated 7/2009

Added 3/1997

**Dose & Administration**

**Oral:** 2 mg/kg per dose every 12 hours for at least 1 week following birth.

**Uses**

Prevention of mother-to-child HIV transmission in neonates born to HIV-infected women who have had no therapy during pregnancy (has received intrapartum therapy only) in combination with zidovudine. In neonates who have received single-dose nevirapine for HIV prophylaxis, lamidudine for at least 7 days after birth may be considered to decrease the risk for nevirapine-resistant HIV infection (United States guidelines). The use of lamivudine with zidovudine for 7 days postpartum is an alternative regimen according to WHO guidelines. The decision to use combination infant antiretroviral prophylaxis, or the treatment of infected infants with combination antiretroviral therapy, should be done in consultation with a pediatric infectious disease expert.

**Monitoring**

Specific monitoring unnecessary due to short treatment course.

**Adverse Effects/Precautions**

Generally well tolerated - limited data in neonates.

**Black Box Warning**

According to the manufacturer's black box warning, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported (in adults).

**Pharmacology**

Lamivudine (3TC) is a synthetic nucleoside analog "prodrug" that inhibits HIV replication by interfering with viral reverse transcriptase. It is intracellularly converted in several steps to the active compound, then renally excreted. Poor CNS penetration, CSF:plasma ratio is 1:100. The oral solution is well-absorbed, with 66% bioavailability in children. The serum half-life in preterm infants less than 33 weeks gestation is approximately 14 hours. Viral resistance develops rapidly to monotherapy with lamivudine (3TC). TMP-SMX increases lamivudine blood levels (significance unknown).

**Special Considerations/Preparation**

Available as an oral solution in concentrations of 5 mg/mL (Epivir-HBV®) and 10 mg/mL (Epivir®). Store at room temperature.

*continued...*

**Selected References**

- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. May 24, 2010. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
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- ◆ Moodley J, Moodley D, Pillay K, et al: Pharmacokinetics and antiretroviral activity of lamivudine alone or when coadministered with zidovudine in human immunodeficiency virus type 1-infected pregnant women and their offspring. *J Infect Dis* 1998;178:1327-1333.
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- ◆ Horneff G, Adams O, Wahn V: Pilot study of zidovudine-lamivudine combination therapy in vertically HIV-infected antiretroviral-naïve children. *AIDS* 1998;12:489-494.
- ◆ Product Information, GlaxoSmithKline, 2008

Uses and References updated 5/2010

Adverse Effects/Precautions updated 1/2009



**Dose & Administration**

10 mg/kg per dose every 8 hours by IV infusion over 30 to 120 minutes.

Preterm newborns less than 1 week of age: 10 mg/kg per dose every 12 hours. Oral dosing is the same as IV.

**Uses**

Limited to treatment of infections, including endocarditis and ventriculitis, caused by gram positive organisms (e.g., methicillin-resistant *Staph. aureus*, penicillin-resistant *Strep. pneumoniae*, and vancomycin-resistant *Enterococcus faecium*) that are refractory to conventional therapy with vancomycin and other antibiotics. Do not use as empiric treatment or in any patient with infections caused by gram-negative organisms.

**Monitoring**

Weekly CBC, AST, ALT. Blood pressure if receiving sympathomimetics.

**Adverse Effects/Precautions**

Elevated transaminases and diarrhea occur in 6 to 10% of treated patients; thrombocytopenia, anemia, and rash occur in 1 to 2%. The FDA issued an alert regarding Zyvox (linezolid) on March 16, 2007. Patients in an open-label, randomized trial comparing linezolid to vancomycin, oxacillin, or dicloxacillin in the treatment of seriously ill patients with intravascular catheter-related bloodstream infections had a higher chance of death than did patients treated with any comparator antibiotic, and the chance of death was related to the type of organism causing the infection. Patients with Gram positive infections had no difference in mortality according to their antibiotic treatment. In contrast, mortality was higher in patients treated with linezolid who were infected with Gram negative organisms alone, with both Gram positive and Gram negative organisms, or who had no infection when they entered the study. See <http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm101503.htm>

**Pharmacology**

Linezolid is an oxazolidinone agent that has a unique mechanism of inhibition of bacterial protein synthesis. It is usually bacteriostatic, although it may be bactericidal against *S. pneumoniae*, *B. fragilis*, and *C. perfringens*. Rapidly penetrates osteoarticular tissues and synovial fluid. CSF concentrations were 70% of plasma concentrations in older patients with non-inflamed meninges. Completely and rapidly absorbed when administered orally to adults and children. Metabolized by oxidation without cytochrome CYP induction. Excreted in the urine as unchanged drug (30%) and two inactive metabolites. Serum half-life in most neonates is 2 to 3 hours, with the exception of preterm neonates less than one week of age, who have a serum half-life of 5 to 6 hours.

*continued...*

**Special Considerations/Preparation**

Linezolid IV injection is supplied as a 2-mg/mL solution in single-use, ready-to-use 100-mL, 200-mL, and 300-mL plastic infusion bags in a foil laminate overwrap. Keep in the overwrap until use. Store at room temperature. Protect from freezing. IV injection may exhibit a yellow color that can intensify over time without affecting potency. An oral suspension is available, 100 mg per 5 mL. Store at room temperature. Use within 21 days after reconstitution. Protect from light.

**Solution Compatibility:** D<sub>5</sub>W, NS, Lactated Ringers.

**Terminal Injection Site Compatibility:** Dex/AA. Acyclovir, amikacin, aminophylline, ampicillin, aztreonam, calcium gluconate, caspofungin, cefazolin, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, esmolol, famotidine, fentanyl, fluconazole, furosemide, ganciclovir, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, lidocaine, lorazepam, magnesium sulfate, meropenem, methylprednisolone, metoclopramide, metronidazole, mezlocillin, midazolam, morphine, naloxone, netilmicin, nicardipine, nitroglycerin, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propranolol, ranitidine, remifentanyl, sodium bicarbonate, theophylline, ticarcillin, tobramycin, vancomycin, vecuronium, and zidovudine.

**Incompatibility:** Amphotericin B, erythromycin lactobionate, phenytoin, and trimethoprim/sulfamethoxazole.

**Selected References**

- ♦ Langgartner M, Mutenthaler A, Haiden N, et al: Linezolid for treatment of catheter-related cerebrospinal fluid infections in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2008;93:F397.
- ♦ Kumar S, Kohlhof S, Valencia G, Hammerschlag MR: Treatment of vancomycin-resistant *Enterococcus faecium* ventriculitis in a neonate. *Int J Antimicrob Agents* 2007;29:740.
- ♦ Tan TQ: Update on the use of linezolid: a pediatric perspective. *Pediatr Infect Dis J* 2004;23:955-956.
- ♦ Jungbluth GL, Welshman IR, Hopkins NK: Linezolid pharmacokinetics in pediatric patients: an overview. *Pediatr Infect Dis J* 2003;23:S153-157.
- ♦ Kearns GL, Jungbluth GL, Abdel-Rahman SM, et al: Impact of ontogeny on linezolid disposition in neonates and infants. *Clin Pharmacol Ther* 2003;74:413-22.
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- ♦ Saiman L, Goldfarb J, Kaplan SA, et al: Safety and tolerability of linezolid in children. *Pediatr Infect Dis J* 2003;22:S193-200.
- ♦ Garges HP, Alexander KA: Newer antibiotics: Linezolid. *NeoReviews* 2003;4:e128-32.
- ♦ Trissel LA, Williams KY, Gilbert DL: Compatibility screening of linezolid injection during simulated Y-site administration with other drugs and infusion solutions. *J Amer Pharm Assoc* 2000;40:515-519.
- ♦ Product information, Pfizer, 2007.

Uses, Compatibilities and References updated 7/2009  
Text updated 3/2007

**Dose & Administration**

**Sepsis:** 20 mg/kg per dose IV.

**Less than 32 weeks GA:**

Less than or equal to 14 days PNA, every 12 hours; greater than 14 days PNA, every 8 hours.

**32 weeks and older GA:**

Less than or equal to 7 days PNA, every 12 hours; greater than 7 days PNA, every 8 hours.

**Meningitis and infections caused by *Pseudomonas* species, all ages:**  
40 mg/kg per dose every 8 hours.

Give as an IV infusion over 30 minutes. Longer infusion times (up to 4 hours) may be associated with improved therapeutic efficacy.

**Uses**

Limited to treatment of pneumococcal meningitis and other serious infections caused by susceptible gram-negative organisms resistant to other antibiotics, especially extended-spectrum beta-lactamase producing *Klebsiella pneumoniae*.

**Monitoring**

Periodic CBC (for thrombocytosis and eosinophilia) and hepatic transaminases. Assess IV site for signs of inflammation.

**Adverse Effects/Precautions**

Diarrhea (4%), nausea/vomiting (1%) and rash (2%). May cause inflammation at the injection site. The use of carbapenem antibiotics can result in the development of cephalosporin resistance in *Enterobacter*, *Pseudomonas*, *Serratia*, *Proteus*, *Citrobacter*, and *Acinetobacter* species. The risks of pseudomembranous colitis and fungal infections are also increased.

**Pharmacology**

Meropenem is a broad-spectrum carbapenem antibiotic that penetrates well into the CSF and most body tissues. It exhibits time-dependent killing of Gram-negative and Gram-positive pathogens, and the goal of therapy is to keep free drug concentrations above the MIC for at least 40% of the dosing interval. It is relatively stable to inactivation by human renal dehydropeptidase. Plasma protein binding is minimal. Clearance is directly related to renal function, and 70% of a dose is recovered intact in the urine. Hepatic function does not affect pharmacokinetics. Serum half-life of meropenem is 3 hours in preterm and 2 hours in full term neonates.

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**Special Considerations/Preparation**

Available (USA) as powder for injection in 500-mg, and 1000-mg vials. Reconstitute with 10 mL of compatible diluent (500 mg vial) or 20 mL (1000 mg vial). When reconstituted with sterile water for injection, stable for up to 2 hours at room temperature or up to 12 hours when refrigerated. When reconstituted with NS to a final concentration between 2.5-50 mg/mL, the solution is stable for up to 2 hours at room temperature or 18 hours when refrigerated. When reconstituted with D5W to final concentration between 2.5-50 mg/mL, the solution is stable for up to 1 hour at room temperature or 8 hours when refrigerated. Solutions prepared in sterile water for injection or NS at concentrations of 1-20 mg/mL are stable in plastic syringes for up to 48 hours when refrigerated. Solutions prepared in D5W at concentrations of 1-20 mg/mL are stable in plastic syringes for up to 6 hours when refrigerated. Solutions prepared for infusion in NS at concentrations of 1-20 mg/mL are stable in plastic IV bags for 4 hours at room temperature or 24 hours when refrigerated. Solutions prepared for infusion in D5W at concentrations of 1-20 mg/mL are stable in plastic IV bags for 1 hour at room temperature or 4 hours when refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Aminophylline, atropine, caspofungin, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, fluconazole, furosemide, gentamicin, heparin, insulin, linezolid, metoclopramide, milrinone, morphine, norepinephrine, phenobarbital, potassium chloride, ranitidine, and vancomycin.

**Incompatibility:** Acyclovir, amphotericin B, calcium gluconate, metronidazole, sodium bicarbonate, and zidovudine.

**Selected References**

- ◆ van den Anker JN, Pokorna P, Kinzig-Schippers M, et al: Meropenem pharmacokinetics in the newborn. *Antimicrob Agents Chemother* 2009;53:3871-3879.
- ◆ Bradley JS, Sauberman JB, Ambrose PG, et al: Meropenem pharmacokinetics, pharmacodynamics, and Monte Carlo Simulation in the neonate. *Pediatr Infect Dis J* 2008;27:794-799.
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- ◆ Patel PR: Compatibility of meropenem with commonly used injectable drugs. *Am J Health-Syst Pharm* 1996;53:2853-55.
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- ◆ Hurst M, Lamb HM: Meropenem: a review of its use in patients in intensive care. *Drugs* 2000;59:653-680.
- ◆ Product Information, Astra-Zeneca, 2007

Dose & Administration and References updated 10/2009

Compatibilities updated 7/2009

Text and References updated 3/2008

**Dose & Administration**

**Loading dose:** 15 mg/kg orally or IV infusion by syringe pump over 60 minutes.

**Maintenance dose:** 7.5 mg/kg per dose orally or IV infusion over 60 minutes. Begin one dosing interval after initial dose.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	Postnatal (days)	Interval (hours)
≤29	0 to 28	48
	>28	24
30 to 36	0 to 14	24
	>14	12
37 to 44	0 to 7	24
	>7	12
≥45	ALL	8

**Uses**

Reserved for treatment of meningitis, ventriculitis, and endocarditis caused by *Bacteroides fragilis* and other anaerobes resistant to penicillin; treatment of serious intra-abdominal infections; and treatment of infections caused by *Trichomonas vaginalis*. Treatment of *C. difficile* colitis.

**Monitoring**

Measure CSF drug concentrations when treating CNS infections. Trough drug concentration should be greater than minimum inhibitory concentration for organism.

**Adverse Effects/Precautions**

Seizures and sensory polyneuropathy have been reported in a few adult patients receiving high doses over a prolonged period. Drug metabolites may cause brownish discoloration of the urine.

**Black Box Warning**

According to the manufacturer's black box warning, metronidazole has been shown to be carcinogenic in mice and rats.

**Pharmacology**

Metronidazole is bactericidal for many anaerobic organisms. It is well absorbed after oral administration, with peak serum concentrations attained in 1 to 3 hours. Distribution in all tissues throughout the body is excellent. It is less than 20% protein bound. Hydroxylation in the liver occurs in term infants and premature infants exposed to antenatal betamethasone. Unchanged drug and the active metabolite are excreted renally. Elimination half-life is strongly related to gestational age, ranging from 22 to 109 hours.

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**Special Considerations/Preparation**

Available in 5 mg/mL concentration in 100 mL single-dose plastic ready-to-use solution containers. **Protect from light** until use and store at controlled room temperature. **Do not refrigerate** (crystals form, but redissolve on warming to room temperature). Osmolarity is 297 mOsm/L, pH is 4.5 to 7. Each container contains 13.5 mEq of sodium.

Supplied as 250-mg and 500-mg tablets for oral administration. Suspension may be prepared by crushing five 250-mg tablets (1250 mg), dissolving powder in 10 mL purified water, then adding cherry syrup to make a total volume of 83 mL. Final concentration is 15 mg/mL.

**Protect from light.** Shake well. Suspension is stable for 30 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, and NS.

**Solution Incompatibility:** Manufacturer recommends that if metronidazole is used with a primary IV fluid system, the primary solution should be discontinued during metronidazole infusion.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, amiodarone, ampicillin, caspofungin, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, clindamycin, dopamine, enalaprilat, esmolol, fluconazole, gentamicin, heparin, hydrocortisone succinate, linezolid, lorazepam, magnesium sulfate, midazolam, milrinone, morphine, netilmicin, nicardipine, penicillin G, piperacillin-tazobactam, prostaglandin E<sub>1</sub>, remifentanyl, and tobramycin.

**Incompatibility:** Aztreonam and meropenem.

**Selected References**

- ◆ Wenisch C, Parschall B, Hasenhundl M, et al: Comparison of vancomycin, teicoplanin, metronidazole, and fusidic acid for the treatment of *Clostridium difficile* - associated diarrhea. *Clin Infect Dis* 1996;22:813.
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- ◆ Oldenburg B, Speck WT: Metronidazole. *Pediatr Clin North Am* 1983;30:71.
- ◆ Jager-Roman E, Doyle PE, Baird-Lambert J, et al: Pharmacokinetics and tissue distribution of metronidazole in the newborn infant. *J Pediatr* 1982;100:651.
- ◆ Product Information, Pfizer, 2010.
- ◆ Product Information, BBraun, 2008.

Special Considerations and References updated 12/2010

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

**Dose & Administration**

7 to 10 mg/kg per dose IV every 24 hours.

The higher dose should be used in the most immature neonates (less than 27 weeks gestation, less than 14 days PNA) and those with meningitis.

IV infusion via syringe pump over at least 1 hour.

**Uses**

Treatment of patients with fungal septicemia, peritonitis, and disseminated infections due to *Candida* species including *C. albicans*, azole-resistant *C. albicans*, and non-albicans species including *C. krusei*, *C. glabrata*, *C. tropicalis* and *C. parapsilosis*.

There are case reports, but no controlled clinical trials, of patients treated for endocarditis and osteomyelitis due to *Candida*. Clinical studies are ongoing for use in neonatal hematogenous *Candida* meningoencephalitis (no data reported yet).

**Monitoring**

Assess IV site for signs of irritation. Periodic measurement of serum potassium, calcium, BUN, hepatic transaminases, and creatinine (isolated renal dysfunction reported in adults).

**Adverse Effects/Precautions**

Limited data in neonates. A case of elevated hepatic transaminases and total bilirubin was reported in a preterm infant exposed perinatally to HIV and hepatitis C infection. Micafungin (8 mg/kg per day) was discontinued after 16 days of treatment and laboratory values gradually declined. The most commonly reported adverse reactions in adults are diarrhea, vomiting, pyrexia, hypokalemia, thrombocytopenia, and histamine-mediated symptoms (including rash, pruritus, facial swelling, and vasodilatation). Rapid infusion rates may result in more frequent histamine-mediated reactions.

**Pharmacology**

Micafungin is a semisynthetic lipopeptide echinocandin antifungal agent with broad-spectrum fungicidal activity against many *Candida* species. It inhibits the synthesis of 1, 3-beta-D-glucan, an integral component of the fungal cell wall. The volume of distribution is relatively high in extremely premature infants, necessitating higher doses. Plasma protein binding is high, primarily to albumin, but it does not displace bilirubin. Pharmacokinetics are linear. Metabolism occurs primarily in the liver through both noncytochrome and cytochrome P450 pathways to 2 biologically inactive metabolites that are eliminated in the feces. Serum half-life ranges from 7 to 16 hours in neonates (mean 11 hours). Mutant strains of *Candida* with reduced susceptibility have been identified in some adult patients during treatment suggesting the potential development of drug resistance. Animal studies suggest tissue penetration to common sites of invasive fungal infections: liver, spleen, kidney, and lungs. No cerebrospinal fluid levels were detected but brain tissue levels were measurable.

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**Special Considerations/Preparation**

Available in single-use lyophilized powder for injection in vials containing 50 and 100 mg. Add 5 mL of 0.9% sodium chloride injection (without bacteriostatic agent) to each 50 mg or 100 mg vial yielding approximately 10 mg or 20 mg per mL, respectively. Inspect reconstituted vials for particulate matter and discoloration prior to administration. Gently dissolve lyophilized powder by swirling the vial to avoid excessive foaming. Do not shake. Protect from light. Reconstituted vials may be stored at room temperature for up to 24 hours before use.

Reconstituted drug should be further diluted in NS or D<sub>5</sub>W to a final concentration between 0.5 to 1.5 mg/mL prior to administration. Diluted infusion should be protected from light and may be stored at room temperature for up to 24 hours before use. An existing IV line should be flushed with NS prior to administration.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Aminophylline, bumetanide, calcium chloride, calcium gluconate, dopamine, esmolol, furosemide, heparin, lidocaine, magnesium sulfate, milrinone, potassium chloride, and sodium nitroprusside.

**Incompatibility:** Albumin, amiodarone, dobutamine, epinephrine, insulin, midazolam, morphine, nicardipine, octreotide, phenytoin, rocuronium, and vecuronium.

**Selected References**

- ◆ Benjamin DK Jr, Smith PB, Arrieta A, et al: Safety and pharmacokinetics of repeat-dose micafungin in young infants. *Clin Pharmacol Ther* 2010;87:93-99.
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- ◆ Product information, Astellas, 2008.

Dose & Administration, References updated 1/2010

Adverse Effects, Monitoring, Compatibilities updated 7/2009

Added 3/2009



**Dose & Administration**

**Cutaneous infections:** Apply small amounts topically to affected areas 3 times daily.

**Decolonization:** Apply small amounts to anterior nares twice daily for 5 to 7 days.

**Uses**

Topical use for skin infections caused by *Staphylococcus aureus*, *S epidermidis*, *S saprophyticus*, and *Streptococcus pyogenes*.

As part of multiple interventions for infection control during MRSA outbreaks in the NICU. Routine use for decolonization is not recommended.

**Monitoring**

Assess affected area for continued infection.

**Adverse Effects/Precautions**

Use only on the skin. No adverse effects reported from topical administration. Routine use may lead to selective bacterial resistance.

**Pharmacology**

Topical antibacterial produced by fermentation of the organism *Pseudomonas fluorescens*. Inhibits protein synthesis by bonding to bacterial isoleucyl-transfer-RNA synthetase. Highly protein bound. Not absorbed into the systemic circulation after topical administration (older infants and children). Metabolized in the skin to an inactive compound and excreted.

**Special Considerations/Preparation**

Available in unit-dose packets and 15 and 30-g tubes as a 2% ointment and cream (20 mg/g).

**Selected References**

- ◆ American Academy of Pediatrics. Staphylococcal Infections. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics 2009; pp 613-615.
- ◆ Khoury J, Jones M, Grim A, et al: Eradication of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit by active surveillance and aggressive infection control measures. *Infect Control Hosp Epidemiol* 2005;26:616-621.
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- ◆ Product Information, OrthoNeutrogena, 2006

References updated 7/2009

Updated 3/2008



**Dose & Administration**

**Usual dosage:** 25 mg/kg per dose IV over 15 minutes.

**Meningitis:** 50 mg/kg per dose.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Treatment of infections caused by penicillinase-producing staphylococci, particularly if evidence of renal dysfunction.

**Monitoring**

Periodic CBC. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Increase dosing interval in patients with hepatic dysfunction. Irritating to veins—watch for phlebitis. Cases of granulocytopenia have been reported.

**Pharmacology**

Inhibits synthesis of bacterial cell wall. Better penetration into CSF than methicillin. Excreted via hepatic clearance.

**Special Considerations/Preparation**

Available in 1 and 2-g vials. Reconstitute 1-g vial with 3.4 mL of sterile water for injection to provide a final volume of 4 mL and a concentration of 250 mg/mL. Also available in 1-g in 50-mL and 2-g in 100-mL frozen single-dose bags. Thaw bags at room temperature or under refrigeration. Do not force thaw by immersing into water baths or microwaving. pH of resulting solution 6 to 8.5. Thawed solution stable for 3 days at room temperature, 21 days refrigerator. Reconstituted solution stable for 3 days at room temperature, 7 days refrigerated. Osmolality was determined to be 709 mOsm/kg of water. For direct intravenous injection, dilute in 15 to 30 mL of NS.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, aminophylline, atropine, chloramphenicol, cimetidine, dexamethasone, enalaprilat, esmolol, famotidine, fentanyl, fluconazole, heparin, lidocaine, magnesium sulfate, morphine, nicardipine, potassium chloride, propofol, sodium bicarbonate, tobramycin, and zidovudine.

**Incompatibility:** Amikacin, aztreonam, gentamicin, hydrocortisone succinate, insulin, methylprednisolone, midazolam, netilmicin, and vancomycin.

### Selected References

- ♦ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ♦ Kitzing W, Nelson JD, Mohs E: Comparative toxicities of methicillin and nafcillin. *Am J Dis Child* 1981;135:52.
- ♦ Banner W, Gooch WM, Burckart G, Korones SB: Pharmacokinetics of nafcillin in infants with low birth weights. *Antimicrob Agents Chemother* 1980;17:691.
- ♦ Product Information, Sandoz, 2004

Compatibilities updated 7/2009

Text updated 3/1997

**Dose & Administration**

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Chart**

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
≤29*	0 to 7	5	48
	8 to 28	4	36
	≥29	4	24
30 to 34	0 to 7	4.5	36
	≥8	4	24
≥35	ALL	4	24

\* or significant asphyxia, PDA, or treatment with indomethacin

**Uses**

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a  $\beta$ -lactam antibiotic.

**Monitoring**

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

**Peak:** 5 to 12 mcg/mL (or  $C_{max}$ /MIC ratio greater than 8:1)

**Trough:** 0.5 to 1 mcg/mL

**Suggested Dosing Intervals**

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤1	≈ 8	24
1.1 to 2.3	≈ 12	36
2.4 to 3.2	≈ 15	48
≥3.3		Measure level in 24 hours

continued...

**Adverse Effects/Precautions**

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

**Pharmacology**

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a  $\beta$ -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of netilmicin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

**Special Considerations/Preparation**

Available in a concentration of 100 mg/mL in 1.5 mL vials. A 10 mg/mL dilution may be made by adding 1 mL of this solution to 9 mL of sterile water for injection. Dilution is stable for 72 hours refrigerated. Do not freeze. **No longer available in the US.**

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Atropine, aztreonam, calcium gluconate, clindamycin, dexamethasone, heparin (concentrations of 1 unit/mL or less), hydrocortisone succinate, iron dextran, isoproterenol, linezolid, metronidazole, norepinephrine, potassium chloride, procainamide, remifentanyl, sodium bicarbonate, and vitamin K<sub>1</sub>.

**Incompatibility:** Ampicillin, furosemide, heparin (concentrations greater than 1 unit/mL), mezlocillin, nafcillin, oxacillin, penicillin G, propofol, and ticarcillin/clavulanate.

*continued...*

**Selected References**

- ◆ Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Stolk LML, Degraeuwe PLJ, Nieman FHM, et al: Population pharmacokinetics and relationship between demographic and clinical variables and pharmacokinetics of gentamicin in neonates. *Ther Drug Monit* 2002;24:527-31.
- ◆ Avent ML, Kinney JS, Istre GR, Whitfield JM: Gentamicin and tobramycin in neonates: comparison of a new extended dosing regimen with a traditional multiple daily dosing regimen. *Am J Perinatol* 2002;8:413-19.
- ◆ Giapros VI, Andronikou S, Cholevas VI, Papadopoulou ZL: Renal function in premature infants during aminoglycoside therapy. *Pediatr Nephrol* 1995;9:163.
- ◆ Daly JS, Dodge RA, Glew RH, et al: Effect of time and temperature on inactivation of aminoglycosides by ampicillin at neonatal dosages. *J Perinatol* 1997;17:42-45.

Compatibilities updated 7/2009

References updated 3/2005





**Dose & Administration**

**Oral:** 2 mg/kg single dose at 48 to 72 hours of age.

If the mother did not receive intrapartum single-dose nevirapine or received the dose within 2 hours prior to delivery, administer 2 mg/kg as soon as possible after birth. Some experts recommend an additional dose at 48 to 72 hours of life under these circumstances.

The addition of at least 7 days of lamivudine may be considered to reduce the risk for nevirapine-resistant HIV virus.

**Uses**

Used **only** in combination with zidovudine in the treatment of neonates born to HIV-infected women who have had no therapy during pregnancy (mother receives zidovudine plus a single 200-mg oral dose of nevirapine during labor). Dosing guidelines above are for prophylactic treatment of neonates born to HIV-infected women. Treatment of infected infants with combination antiretroviral therapy should be done in consultation with a pediatric infectious disease expert.

**Monitoring**

Specific monitoring unnecessary due to short treatment course.

**Adverse Effects/Precautions**

Limited data on toxicity—none reported in neonates.

**Black Box Warning**

According to the manufacturer's black box warning, severe, life-threatening, in some cases fatal, hepatotoxicity and skin reactions have been reported (in adults).

**Pharmacology**

Nevirapine is a non-nucleoside antiretroviral agent that inhibits HIV-1 replication by selectively interfering with viral reverse transcriptase without requiring intracellular metabolism. It also inactivates cell-free virions in the genital tract and breast milk. Synergistic antiviral activity occurs when administered with zidovudine. Nevirapine is rapidly absorbed after oral administration to pregnant women and is highly lipophilic, resulting in therapeutic concentrations being readily transferred across the placenta to the fetus. Serum half-life in the neonates is approximately 44 hours. With the maternal/newborn regimen described above, serum concentrations are above 100 mcg/L throughout the first week of life. Nevirapine is extensively metabolized by, and an inducer of, hepatic CYP3A4 and CYP2B6 isoenzymes. Concomitant administration of phenobarbital or phenytoin, CYP3A inducers, may affect plasma concentrations.

**Special Considerations/Preparation**

Available as an oral suspension in a concentration of 10 mg/mL. Store at room temperature. Shake suspension gently prior to administration.

*continued...*

**Selected References**

- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. May 24, 2010. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
- ◆ Mirochnick M, Dorenbaum A, Blanchard S, et al: Predose infant nevirapine concentration with the two-dose intrapartum neonatal nevirapine regimen: association with timing of maternal intrapartum nevirapine dose. *JAIDS* 2003;33:153-56.
- ◆ Mirochnick M, Clarke DF, Dorenbaum A: Nevirapine: pharmacokinetic considerations in children and pregnant women. *Drugs* 2000;39:281-293.
- ◆ Product Information, Boehringer Ingelheim, 2007

Dose & Administration and References updated 5/2010  
Adverse Effects/Precautions updated 1/2009

**Dose & Administration**

**Topical:** Apply ointment or cream to affected area every 6 hours. Continue treatment for 3 days after symptoms have subsided.

**Oral:** 1 mL (preterm) to 2 mL (term) of 100,000-units/mL suspension divided and applied with swab to each side of mouth every 6 hours. Continue treatment for 3 days after symptoms have subsided.

**Prophylaxis:** 1 mL of 100,000 units/mL suspension orally or instilled into stomach via oro/nasogastric tube 3 times per day.

**Uses**

Treatment of mucocutaneous candidal infections. Prophylaxis against invasive fungal infections in high risk VLBW infants.

**Monitoring**

Assess response to drug.

**Adverse Effects/Precautions**

Possible skin rash caused by vehicle in ointment/cream.

**Pharmacology**

Polyene antifungal similar in structure to amphotericin B. May be fungicidal or fungistatic. Binds to the fungal cell membrane causing disruption of the cell structure. Not absorbed well from the GI tract, skin, or mucous membranes.

**Special Considerations/Preparation**

**Topical ointment/cream:** 100,000 units/g in 15- and 30-g tubes. Ointment dissolved in polyethylene and mineral-oil-gel base.

**Topical powder:** 100,000 units/g in 15- and 30-g plastic squeeze bottles.

**Oral suspension:** 100,000 units/mL in 5-, 60-, and 480-mL bottles. Shake well before applying to mouth. Appears to work best when not mixed with formula. Contains less than 1% alcohol, saccharin, and 50% sucrose.

**Selected References**

- ◆ Ozturk MA, Gunes T, Koklu E, et al: Oral nystatin prophylaxis to prevent invasive candidiasis in neonatal intensive care unit. *Mycoses* 2006;49:484-492.
- ◆ Hoppe JE: Treatment of oropharyngeal candidiasis and candidal diaper dermatitis in neonates and infants: review and reappraisal. *Ped Inf Dis J* 1997;16:885-94.
- ◆ Faix RG, Kovarik SM, Shaw TR, Johnson RV: Mucocutaneous and invasive candidiasis among very low birth weight (<1500 grams) infants in intensive care nurseries: A prospective study. *Pediatrics* 1989;83:101.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 81.
- ◆ Munz D, Powell KR, Pai CH: Treatment of candidal diaper dermatitis: A double-blind placebo-controlled comparison of topical nystatin with topical plus oral nystatin. *J Pediatr* 1982;101:1022.
- ◆ Product Information, Actavis, 2006

Dose/Administration, Uses, and References updated 3/2008



**Dose & Administration**

**Usual dosage:** 25 mg/kg per dose IV over at least 10 minutes.

**Meningitis:** 50 mg/kg per dose.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

**Uses**

Treatment of infections caused by penicillinase-producing staphylococci.

**Monitoring**

Periodic CBC and urinalysis. AST, ALT. Irritating to veins—watch for phlebitis. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Interstitial nephritis associated with hematuria, albuminuria, and casts in urine. Bone marrow depression. Elevated AST and ALT. Hypersensitivity in the form of a rash. Tolerant strains of staphylococci have been reported.

**Pharmacology**

Inhibits synthesis of bacterial cell wall. Rapidly excreted renally unchanged. Poor CSF penetration. Good penetration of pleural, pericardial, and synovial fluids.

**Special Considerations/Preparation**

Available as powder injection in 250-mg, 500-mg, 1-g, 2-g, and 10-g vials. Reconstitute 250 mg vial with 5 mL of sterile water for injection to make a concentration of 50 mg/mL. Reconstituted solution is stable for 4 days at room temperature, 7 days refrigerated. Dilute further using sterile water or NS to a concentration less than or equal to 40 mg/mL. Dilution stable for 4 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, cefotaxime, cefoxitin, chloramphenicol, dopamine, famotidine, fluconazole, heparin, hydrocortisone succinate, magnesium sulfate, milrinone, morphine, potassium chloride, and zidovudine.

**Incompatibility:** Amikacin, caffeine citrate, gentamicin, netilmicin, sodium bicarbonate, and tobramycin.

*continued...*

**Selected References**

- ◆ Maraqa NF, Gomez MM, Rathore MH, Alvarez AM: Higher occurrence of hepatotoxicity and rash in patients treated with oxacillin, compared with those treated with nafcillin and other commonly used antimicrobials. *Clin Infect Dis* 2002;34:50-54.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Nahata MC, Debolt SL, Powell DA: Adverse effects of methicillin, nafcillin, and oxacillin in pediatric patients. *Dev Pharmacol Ther* 1982;4:117.
- ◆ Axline SG, Yaffe SJ, Simon HJ: Clinical pharmacology of antimicrobials in premature infants: II. Ampicillin, methicillin, oxacillin, neomycin, and colistin. *Pediatrics* 1967;39:97.
- ◆ Product Information, Sandoz, 2005

Compatibilities updated 7/2009

Text updated 3/1997

**Dose & Administration**

**\*Use only aqueous crystalline penicillin G for IV administration**  
**Meningitis:** 75,000 to 100,000 units/kg per dose IV infusion over 30 minutes, or IM.

**Bacteremia:** 25,000 to 50,000 units/kg per dose IV infusion over 15 minutes, or IM.

**Group B streptococcal infections:** Some experts recommend using 200,000 units/kg per day for bacteremia and 500,000 units/kg per day for meningitis, in divided doses at more frequent intervals.

**Congenital syphilis:** 50,000 units/kg per dose IV over 15 minutes, given every 12 hours during the first 7 days of life, and every 8 hours thereafter, irrespective of gestational age. Treat for a total of 10 days.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

**Uses**

Treatment of serious infections (bacteremia and meningitis) due to susceptible strains of streptococci (non enterococcal).

Treatment of congenital syphilis. For congenital syphilis, aqueous crystalline penicillin G is recommended in infants with proven or highly probable disease and:

- an abnormal physical examination consistent with congenital syphilis;
- a serum quantitative nontreponemal serologic titer that is fourfold higher than the mother's titer; OR
- a positive darkfield test of body fluid(s).

Also recommended in infants who have a normal physical examination and a serum quantitative nontreponemal titer the same or less than fourfold the maternal titer and the:

- mother was not treated, inadequately treated, or has no documentation of having received treatment;
- mother was treated with erythromycin or another non-penicillin regimen; OR
- mother received treatment less than 4 weeks before delivery.

**Monitoring**

Follow serum sodium and potassium when using high doses and in patients with renal failure. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Cardiac arrest has been reported in patients who received high doses infused rapidly. Significant CNS toxicity has been reported in adults with renal failure who developed CSF concentrations greater than 10 mcg/mL. Bone marrow depression, granulocytopenia, and hepatitis are rare. Hypersensitivity has not been seen in neonates.

*continued...*

## Pharmacology

Inhibits synthesis of bacterial cell wall. Excreted unchanged in the urine. CSF penetration is poor, except in inflamed meninges. Concentrates in joint fluid and urine.

## Special Considerations/Preparation

Aqueous penicillin G is available as powder for injection in two salt forms: penicillin G potassium and penicillin G sodium. Penicillin G potassium contains 1.68 mEq (65.6 mg) potassium per 1 million units, and 0.3 mEq (6.8 mg) sodium per 1 million units. Penicillin G sodium contains 2 mEq (46 mg) sodium per 1 million units. Reconstitute the 5-million unit vial with 8 mL sterile water for injection to make a final concentration of 500,000 units/mL. Reconstituted solution good for 7 days refrigerated. A 100,000 unit/mL dilution may be made by adding 10 mL of reconstituted solution to 40 mL sterile water for injection. Dilution stable for 7 days refrigerated. Penicillin G sodium reconstituted solution stable for 3 days in refrigerator.

Penicillin G potassium is also available as a premixed frozen iso-osmotic solution containing 1, 2 or 3 million units in 50 mL.

**Note:** Penicillin G is also known as benzylpenicillin - do not confuse with benzathine penicillin used for only for IM injections.

1 million units is the equivalent of 600 mg.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, amikacin, amiodarone, caffeine citrate, calcium chloride, calcium gluconate, cefotaxime, cefoxitin, chloramphenicol, cimetidine, clindamycin, dopamine, enalaprilat, erythromycin lactobionate, esmolol, fluconazole, furosemide, gentamicin, heparin, hydrocortisone succinate, lidocaine, magnesium sulfate, metronidazole, morphine, nicardipine, potassium chloride, prostaglandin E<sub>1</sub>, ranitidine and sodium bicarbonate.

**Incompatibility:** Aminophylline, amphotericin B, metoclopramide, netilmicin, pentobarbital, phenytoin, and tobramycin.

## Selected References

- ◆ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010;59(RR-12):1-110.
- ◆ American Academy of Pediatrics. Syphilis. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 644-646.
- ◆ Stoll BJ: Congenital syphilis: evaluation and management of neonates born to mothers with reactive serologic tests for syphilis. *Pediatr Infect Dis J* 1994;13:845.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p45.
- ◆ Pyati SP, Pildes RS, Jacobs NM, et al: Penicillin in infants weighing two kilograms or less with early onset group B streptococcal disease. *N Engl J Med* 1983;308:1383.
- ◆ McCracken GH Jr, Ginsburg C, Chrane DF, et al: Clinical pharmacology of penicillin in newborn infants. *J Pediatr* 1973;82:692.
- ◆ Product Information, Sandoz, 2009
- ◆ Product Information, Sandoz, 2007

Dose & Administration, Uses, and References updated 12/2010  
 Compatibilities updated 7/2009



**Dose & Administration**

**Congenital Syphilis:** 50,000 units/kg/dose IM as a single dose.

**Administration: For IM injection only.** Avoid injection into or near an artery or nerve. Administer by deep IM injection in the midlateral aspect of the thigh. Rotate injection site for repeated administration. Needle may be blocked if injection is not made at a slow, steady rate due to high concentration of suspended material in the product.

**Uses**

Treatment of congenital syphilis in infants during the first month of life. Recommended as an alternative to aqueous crystalline penicillin G or procaine penicillin G in infants who have a normal physical examination and a serum quantitative nontreponemal titer the same or less than fourfold the maternal titer and the:

- mother was not treated, inadequately treated, or has no documentation of having received treatment;
- mother was treated with erythromycin or another non-penicillin regimen; OR
- mother received treatment less than 4 weeks before delivery.

Also recommended in infants whose mother was adequately treated during pregnancy (and treatment given greater than 4 weeks before delivery) and mother has no evidence of reinfection or relapse. Close serologic testing may be used instead of treatment in infants whose mother's nontreponemal titers decreased fourfold after appropriate therapy for early syphilis and remained stable or low for late syphilis. For infants whose mother's treatment was adequate before pregnancy and nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (VDRL less than 1:2; RPR less than 1:4), no treatment is required; however, it may be considered if follow-up is not assured.

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, inadvertent intravenous administration of penicillin G benzathine (to be given IM only) has been associated with cardiorespiratory arrest and death.

Serious and potentially fatal hypersensitivity reactions have occurred. The Jarisch-Hersheimer reaction (fever, chills, myalgia, headache, tachycardia, hyperventilation, mild hypotension) may occur after initiation of therapy in patients with syphilis. Avoid intravenous or intra-arterial administration, or injection into or near a nerve; severe neurovascular damage (transverse myelitis with permanent paralysis, gangrene requiring amputation, and necrosis and sloughing at or around injection site) has occurred, especially in infants. Quadriceps femoris fibrosis and atrophy have occurred following repeated intramuscular administration into the anterolateral thigh.

**Pharmacology**

Inhibits synthesis of bacterial cell wall. Dissolves slowly at site of injection with hydrolysis to penicillin G. Distributes widely into body tissues. Highest concentration in the kidneys, with smaller amounts in the liver, skin, and intestines. Approximately 60% bound to serum protein. Excreted rapidly by tubular excretion. In young infants and patients with renal impairment, excretion is prolonged.

*continued...*

## Special Considerations/Preparation

Available in a concentration of 600,000 units/mL in 1-, 2-, and 4-mL syringes. **Store in refrigerator. Do not freeze.**

## Selected References

- ◆ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010;59(RR-12):1-110.
- ◆ Product Information: Bicillin L-A, penicillin G benzathine injection, suspension, King Pharmaceuticals, 2009.

Added 02/2011

**Dose & Administration**

**Congenital Syphilis:** 50,000 units/kg/dose IM once daily for 10 days.

**Administration: For IM injection only.** Avoid injection into or near an artery or nerve. Administer by deep IM injection in the midlateral aspect of the thigh. Rotate injection site for repeated administration. Needle may be blocked if injection is not made at a slow, steady rate due to high concentration of suspended material in the product.

**Uses**

Treatment of congenital syphilis in infants during the first month of life. For congenital syphilis, procaine penicillin G is recommended as an alternative to aqueous crystalline penicillin G in infants with proven or highly probable disease and:

- an abnormal physical examination consistent with congenital syphilis;
- a serum quantitative nontreponemal serologic titer that is fourfold higher than the mother's titer; OR
- a positive darkfield test of body fluid(s).

Also recommended as an alternative to aqueous crystalline penicillin G in infants who have a normal physical examination and a serum quantitative nontreponemal titer the same or less than fourfold the maternal titer and the:

- mother was not treated, inadequately treated, or has no documentation of having received treatment;
- mother was treated with erythromycin or another non-penicillin regimen; OR
- mother received treatment less than 4 weeks before delivery.

**Monitoring**

Periodic monitoring of CBC and renal function is recommended.

**Adverse Effects/Precautions**

Serious and potentially fatal hypersensitivity reactions have occurred. Avoid intravenous or intra-arterial administration, or injection into or near a nerve; severe neurovascular damage (transverse myelitis with permanent paralysis, gangrene requiring amputation, and necrosis and sloughing at or around injection site) has occurred, especially in infants. Quadriceps femoris fibrosis and atrophy have occurred following repeated intramuscular administration into the anterolateral thigh. Prolonged therapy may lead to an increased risk of neutropenia and serum sickness-like reactions.

**Pharmacology**

Inhibits synthesis of bacterial cell wall. Equimolecular compound of procaine and penicillin G is a suspension. Dissolves slowly at site of injection, with maximum blood level at approximately 4 hours, declining slowly over a period of 15 to 20 hours. Distributes widely into body tissues. Highest concentration in the kidneys, with smaller amounts in the liver, skin, and intestines. Approximately 60% bound to serum protein. Excreted rapidly by tubular excretion. In young infants and patients with renal impairment, excretion is prolonged. Approximately 60% to 90% of a dose is excreted in the urine within 24 to 36 hours.

*continued...*

## Special Considerations/Preparation

Available in a concentration of 600,000 units/mL in 1-, 2-, and 4-mL syringes. **Store in refrigerator. Do not freeze.**

## Selected References

- ◆ Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2010. *MMWR* 2010;59(RR-12):1-110.
- ◆ Product Information: Penicillin G procaine injectable suspension, King Pharmaceuticals, 2006.

Added 02/2011

**Dose & Administration**

50 to 100 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Semisynthetic penicillin with increased activity against *Pseudomonas aeruginosa* and many strains of *Klebsiella*, *Serratia*, *E coli*, *Enterobacter*, *Citrobacter*, and *Proteus*. Also effective against group B *Streptococcus*.

**Monitoring**

Desired peak serum concentration is approximately 150 mcg/mL. Desired trough concentration ranges from 15 to 50 mcg/mL (available as bioassay). Peak serum concentration is lower with IM administration. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine.

**Pharmacology**

Piperacillin is a potent, broad-spectrum, semi-synthetic, ureidopenicillin possessing high activity against gram-negative bacteria. Inactivation by beta-lactamase-producing bacteria. Synergistic with aminoglycosides. Good penetration into bone; CSF penetration similar to that of other penicillins. Serum half-life depends on gestational age and postnatal age. Primarily excreted renally unchanged.

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**Special Considerations/Preparation**

Available as powder for injection in 2-g, 3-g, 4-g, and 40-g vials. Reconstitute 2-g vial with 10 mL of sterile water for injection to make a final concentration of 200 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 2 days refrigerated. A 50 mg/mL dilution may be made by adding 2.5 mL of reconstituted solution to 7.5 mL sterile water for injection. Dilution stable for 2 days refrigerated.

**IM Administration :** Use 400 mg/mL concentration.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, aminophylline, aztreonam, clindamycin, enalaprilat, esmolol, famotidine, heparin, hydrocortisone succinate, linezolid, lorazepam, magnesium sulfate, midazolam, milrinone, morphine, nicardipine, potassium chloride, propofol, ranitidine, remifentanyl, and zidovudine.

**Incompatibility:** Amikacin, amiodarone, gentamicin, netilmicin, fluconazole, tobramycin, and vancomycin.

**Selected References**

- ◆ Kacet N, Roussel-Delvallez M, Gremillet C, et al: Pharmacokinetic study of piperacillin in newborns relating to gestational and postnatal age. *Pediatr Infect Dis J* 1992;11:365.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Reed MD, Myers CM, Yamashita TS, Blumer JL: Developmental pharmacology and therapeutics of piperacillin in gram-negative infections. *Dev Pharmacol Ther* 1986;9:102.
- ◆ Placzek M, Whitelaw A, Want S, et al: Piperacillin in early neonatal infection. *Arch Dis Child* 1983;58:1006-1009.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006

Compatibilities updated 7/2009

Updated 3/2008

**Dose & Administration**

50 to 100 mg/kg per dose (as piperacillin component) IV infusion by syringe pump over 30 minutes.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	8

**Uses**

Treatment of non-CNS infections, caused by susceptible beta-lactamase producing bacteria, including many strains of *E. coli*, *Enterobacter*, *Klebsiella*, *Haemophilus influenzae*, *Proteus mirabilis*, *Pseudomonas spp.*, and *Staph. aureus*. Also effective against group B *Streptococcus*.

**Monitoring**

Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine.

**Pharmacology**

Zosyn® combines the extended-spectrum antibiotic piperacillin with the beta-lactamase inhibitor tazobactam in a 8:1 ratio. Piperacillin is primarily eliminated unchanged by renal mechanisms, whereas tazobactam undergoes significant hepatic metabolism. The mean half-life of piperacillin and tazobactam in neonates is approximately 1.5 hours. CNS penetration is modest (limited data). Sodium content is 2.35 mEq per gram of piperacillin.

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**Special Considerations/Preparation**

Available as powder for injection (containing EDTA and sodium citrate) in 2.25-g, 3.375-g, and 4.5-g vials. Reconstitute 2.25-g vial with 10 mL of sterile water for injection to make a concentration of 200 mg/mL piperacillin. Reconstituted solution stable for 24 hours at room temperature, 48 hours refrigerated. pH 4.5 to 6.8. Each 2.25-g vial contains 2.79 mEq (64 mg) of sodium per gram of piperacillin. Dilute reconstituted solution further to a final concentration of 50 mg/mL (some sources recommend 20 mg/mL) using compatible solution.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, NS and LR.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Aminophylline, aztreonam, bumetanide, calcium gluconate, cefepime, cimetidine, clindamycin, dexamethasone, dopamine, enalaprilat, esmolol, fluconazole, furosemide, heparin, hydrocortisone succinate, linezolid, lorazepam, magnesium sulfate, metoclopramide, metronidazole, milrinone, morphine, potassium chloride, ranitidine, remifentanyl, sodium bicarbonate, trimethoprim-sulfamethoxazole, and zidovudine.

**Incompatibility:** Acyclovir, amikacin, amiodarone, amphotericin B, azithromycin, caspofungin, dobutamine, famotidine, ganciclovir, gentamicin, netilmicin, tobramycin, and vancomycin.

**Selected References**

- ◆ Pillay T, Pillay DG, Adhikari M, Sturn AW: Piperacillin/tazobactam in the treatment of Klebsiella pneumoniae infections in neonates. *Am J Perinatol* 1998;15:47-51.
- ◆ Reed MD, Goldfarb J, Yamashita TS, Blumer JL: Single dose pharmacokinetics of piperacillin and tazobactam in infants and children. *Antimicrob Agents Chemother* 1994;38:2817-26.
- ◆ Schoonover L, Occhipinti D, Rodvold K, et al: Piperacillin/tazobactam: A new beta-lactam/beta-lactamase inhibitor combination. *Ann Pharmacother* 1995;29:501-14.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Product Information, Wyeth, 2007

Compatibilities updated 7/2009

Text updated 3/2008

Added 3/2003



**Dose & Administration**

7.5 mg/kg/dose every 12 hours by IV infusion over 60 minutes.  
Administration via a central catheter is recommended.

**Uses**

Limited to treatment of infections caused by gram positive organisms resistant to other antibiotics, e.g. methicillin-resistant *Staph. aureus* and vancomycin-resistant *Enterococcus faecium* (not *E faecalis*).

**Monitoring**

Periodic measurement of serum bilirubin and transaminases. Assess peripheral IV site for signs of inflammation.

**Adverse Effects/Precautions**

Myalgias and arthralgias occur frequently in adults with hepatic or renal failure. Elevations in serum bilirubin and transaminases are common. Diarrhea and rash occur infrequently.

**Pharmacology**

No data are available for infants. Synercid® is a parenteral antimicrobial agent which consists of two streptogramin antibiotics (quinupristin and dalfopristin in a 30:70 ratio) that inhibit bacterial protein synthesis by binding to separate sites on the bacterial ribosome. Serum half-life of quinupristin in adults ranges from 1 to 3 hours, and of dalfopristin ranges from 5 to 9 hours. Seventy-five percent is excreted via the biliary route.

**Special Considerations/Preparation**

Synercid® is supplied as a lyophilized powder in single-dose, 10-mL vials containing 500 mg or 600 mg. Store refrigerated. Reconstitute 500-mg and 600-mg vials by adding 5 mL or 6 mL of Sterile Water for Injection or D<sub>5</sub>W, respectively, resulting in a concentration of 100 mg/mL. Reconstituted solution should be diluted within 30 minutes. Before administration, dilute with D<sub>5</sub>W to a concentration of 2 mg/mL. A concentration up to 5 mg/mL may be used for central lines. Concentrations less than 1 mg/mL may be used if venous irritation occurs following peripheral administration. Diluted solution is stable for 5 hours at room temperature, or 54 hours if stored under refrigeration. **Do not freeze.**

**Solution Compatibility:** D<sub>5</sub>W.

**Solution Incompatibility:** NS.

**Terminal Injection Site Compatibility:** Aztreonam, fluconazole, metoclopramide, and potassium chloride.

**Selected References**

- ◆ Loeffler AM, Drew RH, Perfect JR, et al: Safety and efficacy of quinupristin/dalfopristin for treatment of invasive Gram-positive infections in pediatric patients. *Pediatr Infect Dis J* 2002;21:950-56.
- ◆ Gray JW, Darbyshire PJ, Beath SV, et al: Experience with quinupristin/dalfopristin in treating infections with vancomycin-resistant *Enterococcus faecium* in children. *Pediatr Infect Dis J* 2000;19:234-238.
- ◆ Lamb HM, Figgitt DP, Faulds D: Quinupristin/Dalfopristin: A review of its use in the management of serious gram-positive infections. *Drugs* 1999;58:1061-1097.
- ◆ Product Information, Monarch Pharmaceuticals, 2010.

Special Considerations and References updated 12/2010



**Dose & Administration**

**Oral:** 10 to 20 mg/kg per dose every 24 hours. May administer with feedings.

**IV:** 5 to 10 mg/kg per dose every 12 hours, given via syringe pump over 30 minutes.

**Do not administer IM or SC.**

**Prophylaxis for high-risk contacts of invasive meningococcal disease:** 5 mg/kg per dose orally every 12 hours, for 2 days.

**Prophylaxis for high-risk contacts of invasive *H influenzae* type b disease:** 10 mg/kg per dose orally every 24 hours, for 4 days.

**Uses**

Used in combination with vancomycin or aminoglycosides for treatment of persistent staphylococcal infections. Prophylaxis against infections caused by *N meningitidis* and *H influenzae* type b.

**Monitoring**

Monitor hepatic transaminases and bilirubin. Periodic CBC for thrombocytopenia. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Causes orange/red discoloration of body secretions (e.g. sweat, urine, tears, sputum). Extravasation may cause local irritation and inflammation. Rifampin is a potent inducer of several cytochrome P450 enzymes. If administered concomitantly, the following drugs may have decreased pharmacologic effects due to increased metabolism: aminophylline, amiodarone, ecimetidine, corticosteroids, digoxin, enalapril, fluconazole, midazolam, morphine, phenobarbital, phenytoin, propranolol, and zidovudine.

**Pharmacology**

Rifampin is a semisynthetic antibiotic with a wide spectrum of antibacterial activity against staphylococci, most streptococci, *H influenzae*, *Neisseria* sp., *Legionella*, *Listeria*, some *Bacteroides* species, *Mycobacterium tuberculosis*, and certain atypical mycobacterium. Enterococci and aerobic gram-negative bacilli are generally resistant. Not used as monotherapy because resistance may develop during therapy. Inhibits transcription of DNA to RNA by binding to the beta subunit of bacterial RNA-polymerase. Well absorbed orally. Rapidly deacetylated to desacetyl-rifampin (active metabolite) and undergoes enterohepatic circulation. Nearly all of the rifampin excreted into the bile is deacetylated within 6 hours. Serum half-life ranges from 1 to 3 hours.

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**Special Considerations/Preparation**

Available as a lyophilized powder for injection in 600-mg vials. Reconstitute with 10 mL of sterile water for injection to make a final concentration of 60 mg/mL. Reconstituted solution is stable for 24 hours at room temperature. Further dilution is required - maximum concentration for infusion is 6 mg/mL. A 3 mg/mL dilution may be made by adding 0.5 mL of reconstituted solution to 9.5 mL of NS or D<sub>5</sub>W. Dilution made with NS is stable for 24 hours at room temperature. Dilution made with D<sub>5</sub> W is stable for 4 hours at room temperature. Do not use if solution precipitates.

A neonatal suspension may be prepared by mixing 5 mL (300 mg) of the reconstituted IV solution with 25 mL of simple syrup to make a final concentration of 10 mg/mL. Shake well before use. Suspension is stable for 4 weeks at room temperature or refrigerated. Also available in 150- and 300-mg capsules. Preparation of oral suspension using capsules yields variable dosage bioavailability.

**Solution Compatibility:** D<sub>5</sub>W and NS. No data available on Dex/AA or fat emulsion.

**Terminal Injection Site Compatibility:** No data available.

**Selected References**

- ◆ Shama A, Patole SK, Whitehall JS: Intravenous rifampicin in neonates with persistent staphylococcal bacteraemia. *Acta Paediatr* 2002;91:670-673.
- ◆ Fernandez M, Rench MA, Albany EA, Edwards MS: Failure of rifampin to eradicate group B streptococcal colonization in infants. *Pediatr Infect Dis J* 2001;20:371-376.
- ◆ Tan TQ, Mason EO, Ou C-N, et al: Use of intravenous rifampin in neonates with persistent staphylococcal bacteremia. *Antimicrob Agents Chemother* 1993;37:2401.
- ◆ Koup JR, William-Warren J, Viswanathan CT, et al: Pharmacokinetics of rifampin in children. II. Oral bioavailability. *Ther Drug Monit* 1986;8:17.
- ◆ Koup JR, William-Warren J, Weber A, et al: Pharmacokinetics of rifampin in children. I. Multiple dose intravenous infusion. *Ther Drug Monit* 1986;8:11.
- ◆ McCracken GH, Ginsburg CM, Zweighaft TC, et al: Pharmacokinetics of rifampin in infants and children: relevance to prophylaxis against Haemophilus influenzae type B disease. *Pediatrics* 1980;66:17.
- ◆ Nahata MC, Morosco RS, Hipple TF: Effect of preparation method and storage on rifampin concentration in suspensions. *Ann Pharmacother* 1994;28:182.
- ◆ Product Information, Bedford, 2004

IV dose and References updated 3/2005.

**Dose & Administration**

75 to 100 mg/kg per dose IV infusion by syringe pump over 30 minutes.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Treatment of non-CNS infections, caused by susceptible  $\beta$ -lactamase producing bacteria, including many strains of *E. coli*, *Enterobacter*, *Klebsiella*, *Haemophilus influenzae*, *Proteus mirabilis*, *Pseudomonas spp.*, and *Staph. aureus*.

**Monitoring**

Serum concentrations are not routinely monitored. Assess renal function prior to therapy. Measure serum sodium concentrations and hepatic transaminases periodically. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine. Hyponatremia may be exacerbated in ELBW patients.

**Pharmacology**

Timentin® combines the extended-spectrum antibiotic ticarcillin with the  $\beta$ -lactamase inhibitor clavulanic acid in a 30:1 ratio. Ticarcillin is primarily eliminated unchanged by renal mechanisms, whereas clavulanate undergoes significant hepatic metabolism. As a result the mean half-life of ticarcillin in neonates is 4.2 hours compared to a mean half-life of 2 hours for clavulanate. CNS penetration is modest (limited data). Sodium content is 4.75 mEq per gram, therefore each dose will contain 0.35 to 0.48 mEq per kg body weight.

continued...

**Special Considerations/Preparation**

Available as powder for injection in 3.1-g vials. Reconstitute vial by adding 13 mL of sterile water for injection. Dilute further with a compatible solution to a concentration between 10 and 100 mg/mL. Dilutions are stable for 24 hours at room temperature, 3 days refrigerated (D5W), and 7 days refrigerated (NS and LR). Frozen dilutions stable for 7 days for D5W and 30 days for NS and LR.

**Solution Compatibility:** D<sub>5</sub>W, LR, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Aztreonam, cefepime, famotidine, fluconazole, heparin, insulin, milrinone, morphine, propofol, remifentanyl, and theophylline.

**Incompatibility:** Amikacin, azithromycin, gentamicin, netilmicin, sodium bicarbonate, tobramycin, and vancomycin.

**Selected References**

- ◆ Rubino CM, Gal P, Ransom JL: A review of the pharmacokinetic and pharmacodynamic characteristics of  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combination antibiotics in premature infants. *Pediatr Infect Dis J* 1998;17:1200-1210.
- ◆ Reed MD: A reassessment of ticarcillin/clavulanic acid dose recommendations for infants, children, and adults. *Pediatr Infect Dis J* 1998;17:1195-1199.
- ◆ Product Information, GlaxoSmithKline, 2007.

Compatibilities updated 7/2009

Added 3/2002

**Dose & Administration**

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Chart**

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
≤29*	0 to 7	5	48
	8 to 28	4	36
	≥29	4	24
30 to 34	0 to 7	4.5	36
	≥8	4	24
≥35	ALL	4	24

\* or significant asphyxia, PDA, or treatment with indomethacin

**Uses**

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a  $\beta$ -lactam antibiotic.

**Monitoring**

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

**Peak:** 5 to 12 mcg/mL (or  $C_{max}/MIC$  ratio greater than 8:1)

**Trough:** 0.5 to 1 mcg/mL

**Suggested Dosing Intervals**

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤1	~ 8	24
1.1 to 2.3	~ 12	36
2.4 to 3.2	~ 15	48
≥3.3		Measure level in 24 hours

continued...

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

**Pharmacology**

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a  $\beta$ -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of tobramycin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

**Special Considerations/Preparation**

Pediatric injectable solution available in a concentration of 10 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Acyclovir, alprostadiol, amiodarone, aztreonam, calcium gluconate, cefoxitin, ceftazidime, clindamycin, dopamine, enalaprilat, esmolol, fluconazole, furosemide, insulin, heparin (concentrations of 1 unit/mL or less), linezolid, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, nafcillin, nifedipine, ranitidine, remifentanyl, theophylline, and zidovudine.

**Incompatibility:** Ampicillin, azithromycin, cefepime, imipenem/cilastatin, indomethacin, heparin (concentrations greater than 1 unit/mL), mezlocillin, oxacillin, penicillin G, propofol, and ticarcillin/clavulanate.

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**Selected References**

- ◆ Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Avent ML, Kinney JS, Istre GR, Whitfield JM: Gentamicin and tobramycin in neonates: comparison of a new extended dosing regimen with a traditional multiple daily dosing regimen. *Am J Perinatol* 2002;8:413-19.
- ◆ de Hoog M, Schoemaker RC, Mouton JW, van den Anker JN: Tobramycin population pharmacokinetics in neonates. *Clin Pharmacol Ther* 1997;62:392-399.
- ◆ Giapros VI, Andronikou S, Cholevas VI, Papadopoulou ZL: Renal function in premature infants during aminoglycoside therapy. *Pediatr Nephrol* 1995;9:163.
- ◆ Daly JS, Dodge RA, Glew RH, et al: Effect of time and temperature on inactivation of aminoglycosides by ampicillin at neonatal dosages. *J Perinatol* 1997;17:42-45.
- ◆ Williams BS, Ransom JL, Gal P, et al: Gentamicin pharmacokinetics in neonates with patent ductus arteriosus. *Crit Care Med* 1997;25:273-275.
- ◆ Product Information, Hospira, 2005

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

Dosing, Compatibilities, and References updated 3/2007



**Dose & Administration**

16 mg/kg per dose orally every 12 hours.

Treat for a minimum of 6 weeks; longer-term treatment may be appropriate.

Note: Dosing applies only to pharmaceutical grade valganciclovir. Data are not available for extemporaneous formulations.

**Uses**

Treatment of infants with symptomatic congenital CMV infections.

**Monitoring**

Periodic CBC; periodic assessment of viral load.

**Adverse Effects/Precautions**

Neutropenia occurs frequently. If Absolute Neutrophil Count (ANC) less than 500 cells/mm<sup>3</sup>, hold drug until ANC greater than 750 cells/mm<sup>3</sup>. If the ANC falls again to less than 750 cells/mm<sup>3</sup>, reduce the dosage by 50%. If ANC again falls to less than 500 cells/mm<sup>3</sup>, discontinue the drug.

**Black Box Warning**

The clinical toxicity of valganciclovir, which is metabolized to ganciclovir, includes granulocytopenia, anemia, and thrombocytopenia. Animal data indicate that ganciclovir is mutagenic, teratogenic, and carcinogenic.

**Pharmacology**

Valganciclovir is a prodrug of ganciclovir that is rapidly converted to ganciclovir after oral administration by liver and intestinal esterases. Bioavailability is 40% to 60%, and may be improved by administering with food. Excreted entirely by the kidneys as unchanged drug. Elimination half-life in infants is 3 hours. Dosing adjustments may be required for infants with renal impairment.

**Special Considerations/Preparation**

Valcyte® is supplied as a white to slightly yellow powder for constitution, forming a colorless to brownish yellow tutti-frutti flavored solution, which when constituted with water as directed contains 50 mg/mL valganciclovir free base. Available in glass bottles containing approximately 100 mL of solution after constitution. The inactive ingredients of Valcyte for oral solution are sodium benzoate, fumaric acid, povidone K-30, sodium saccharin, mannitol and tutti-frutti flavoring.

Valcyte® for oral solution must be constituted by the pharmacist prior to dispensing to the patient. To prepare the oral solution, measure 91 mL of purified water in a graduated cylinder. Shake the bottle to loosen the powder. Add approximately half the total amount of water for constitution to the bottle and shake well for about 1 minute. Add the remainder of water and shake well for about 1 minute. This prepared solution contains 50 mg of valganciclovir free base per 1 mL. Store constituted oral solution under refrigeration at 2°C to 8°C (36°F to 46°F) for no longer than 49 days. Do not freeze.

*continued...*

**Selected References**

- ♦ Marshall BC, Koch WC: Antivirals for cytomegalovirus infection in neonates and infants. *Pediatr Drugs* 2009;11:309-321.
- ♦ Kimberlin DW, Acosta EP, Sanchez PJ, et al. Pharmacokinetic and pharmacodynamic assessment of oral valganciclovir in the treatment of symptomatic congenital cytomegalovirus disease. *J Infect Dis* 2008; 197:836-45.
- ♦ Michaels MG: Treatment of congenital cytomegalovirus: where are we now? *Expert Rev Anti Infect Ther* 2007;5:441-448.
- ♦ Product Information, Roche, 2009.

Added 1/2010

**Dose & Administration**

IV infusion by syringe pump over 60 minutes.

**Meningitis:** 15 mg/kg per dose

**Bacteremia:** 10 mg/kg per dose

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 14	18
	>14	12
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6

**Uses**

Drug of choice for serious infections caused by methicillin-resistant staphylococci (e.g. *S aureus* and *S epidermidis*) and penicillin-resistant pneumococci.

**Monitoring**

Serum trough concentrations should be followed in neonates because of changes in renal function related to maturation and severity of illness. Peak concentrations have not been clearly demonstrated to correlate with efficacy, but monitoring these has been recommended when treating meningitis.

**Trough:** 5 to 10 mcg/mL for most infections. Many experts recommend 15 to 20 mcg/mL when treating MRSA pneumonia, endocarditis, or bone/joint infections.

**Peak:** 30 to 40 mcg/mL when treating meningitis

(Draw 30 minutes after end of infusion.)

Assess renal function. Observe IV site for signs of extravasation and phlebitis.

**Adverse Effects/Precautions**

**Nephrotoxicity and ototoxicity:** Enhanced by aminoglycoside therapy.

**Rash and hypotension (red man syndrome):** Appears rapidly and resolves within minutes to hours. Lengthening infusion time usually eliminates risk for subsequent doses.

**Neutropenia:** Reported after prolonged administration (more than 3 weeks).

**Phlebitis:** May be minimized by slow infusion and dilution of the drug.

**Pharmacology**

Vancomycin is bactericidal for most gram-positive bacteria, but bacteriostatic for enterococci. It interferes with cell wall synthesis, inhibits RNA synthesis, and alters plasma membrane function. Killing activity is primarily a time-dependent process, not concentration-dependent. MICs for sensitive organisms are less than or equal to 1 mcg/mL. Diffusion into the lung and bone is variable. CSF concentrations in premature infants ranged from 26% to 68% of serum

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concentrations. Protein binding is as high as 50% in adults. Elimination is primarily by glomerular filtration, with a small amount of hepatic metabolism.

### Special Considerations/Preparation

Available as powder for injection in 500-mg and 1-g vials. Reconstitute 500-mg and 1-g vial with 10 mL and 20 mL of sterile water for injection, respectively, to make a final concentration of 50 mg/mL. Reconstituted solution stable for 4 days refrigerated. Dilute prior to administration using D<sub>5</sub>W or NS to a maximum concentration of 5 mg/mL (concentrations up to 10 mg/mL may also be used in fluid restricted patients).

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, alprostadil, amikacin, ampicillin, aminophylline, amiodarone, aztreonam, caffeine citrate, calcium gluconate, caspofungin, cimetidine, enalaprilat, esmolol, famotidine, fluconazole, heparin (concentrations of 1 unit/mL or less), hydrocortisone succinate, insulin, linezolid, lorazepam, magnesium sulfate, meropenem, midazolam, milrinone, morphine, nicardipine, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanyl, sodium bicarbonate, vecuronium, and zidovudine.

**Incompatibility:** Cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, dexamethasone, heparin (concentrations greater than 1 unit/mL), mezlocillin, nafcillin, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, ticarcillin, and ticarcillin/clavulanate.

### Selected References

- ◆ Liu C, Bayer A, Cosgrove SE, et al: Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1-38.
- ◆ Hidayat LK, Hsu DI, Quist R, et al: High-dose vancomycin therapy for methicillin-resistant *Staphylococcus aureus* infections. *Arch Intern Med* 2006;166:2138-2144.
- ◆ de Hoog M, Schoemaker RC, Mouton JW, van den Anker JN: Vancomycin population pharmacokinetics in neonates. *Clin Pharmacol Ther* 2000;67:360-367.
- ◆ Ahmed A: A critical evaluation of vancomycin for treatment of bacterial meningitis. *Pediatr Infect Dis J* 1997;16:895-903.
- ◆ Trissel LA, Gilbert DL, Martinez JF: Concentration dependency of vancomycin hydrochloride compatibility with beta-lactam antibiotics during simulated y-site administration. *Hosp Pharm* 1998;33:1515-1520.
- ◆ Reiter PD, Doron MW: Vancomycin cerebrospinal fluid concentrations after intravenous administration in premature infants. *J Perinatol* 1996;16:331-335.
- ◆ Schilling CG, Watson DM, McCoy HG, Uden DL: Stability and delivery of vancomycin hydrochloride when admixed in a total parenteral nutrition solution. *JPEN* 1989;13:63.
- ◆ Lacouture PG, Epstein MF, Mitchell AA: Vancomycin-associated shock and rash in newborn infants. *J Pediatr* 1987;111:615.
- ◆ Schaible DH, Rocci ML, Alpert GA, et al: Vancomycin pharmacokinetics in infants: Relationships to indices of maturation. *Pediatr Infect Dis* 1986;5:304.
- ◆ Product Information, APP Pharmaceuticals, 2008.

Special Considerations and References updated 2/2011

Compatibilities updated 7/2009

Monitoring updated 3/2008

NEOFAX® 2011

**Dose & Administration**

**IV:** 1.5 mg/kg per dose, given via infusion pump over 1 hour.

**Oral:** 2 mg/kg per dose.

**Do not administer IM.**

May administer with food, although manufacturer recommends administration 30 minutes before or 1 hour after a meal.

Begin treatment within 6 to 12 hours of birth, and continue for 6 weeks. Initiation of post-exposure prophylaxis after the age of 2 days is not likely to be effective. Subsequent treatment is based on antiretroviral drug resistance testing.

To use the dosing chart, please refer to explanatory note on page 1.

**Dosing Interval Chart**

Gestational Age (weeks)	Postnatal Age (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 34	0 to 14 >14	12 8
≥35	ALL	6

**Uses**

Dosing guidelines above are for prophylactic treatment of neonates born to HIV-infected women. Treatment of infants with combination antiretroviral therapy should be done in consultation with a pediatric infectious disease expert.

**Monitoring**

CBC at the beginning of therapy, then every other week to assess for anemia, thrombocytopenia, and neutropenia.

**Adverse Effects/Precautions**

Anemia and neutropenia occur frequently, and are associated with serum concentrations greater than 3 micromol/L. Mild cases usually respond to a reduction in dose. Severe cases may require cessation of treatment and/or transfusion. Bone marrow toxicity may be increased by concomitant administration of acyclovir, ganciclovir, and TMP-SMX. Lactic acidemia is common in infants exposed to in utero highly active antiretroviral therapy. Concomitant treatment with fluconazole or methadone significantly reduces zidovudine metabolism - dosing interval should be prolonged.

**Black Box Warning**

According to the manufacturer's black box warning, zidovudine has been associated with hematologic toxicity, including neutropenia and severe anemia, particularly in patients with advanced HIV disease. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported (in adults).

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### Pharmacology

Zidovudine is a nucleoside analog that inhibits HIV replication by interfering with viral reverse transcriptase. It is converted intracellularly in several steps to a triphosphate derivative, metabolized via hepatic glucuronidation, then renally excreted. Protein binding is approximately 25%. Zidovudine distributes into cells by passive diffusion and is relatively lipophilic. The CSF: plasma ratio is 0.24. The relationship between serum concentration and clinical efficacy is unclear. The oral syrup is well-absorbed, but only 65% bioavailable due to significant first-pass metabolism. The serum half-life in term newborns is 3 hours, declining to 2 hours after 2 weeks of age. In preterm infants less than 33 weeks gestation, half-life during the first two weeks of life ranges from 5 to 10 hours, decreasing to 2 to 6 hours afterward.

### Special Considerations/Preparation

Available as a syrup for oral use in a concentration of 10 mg/mL.

The IV form is supplied in a concentration of 10 mg/mL in a 20 mL single-use vial. **Dilute before IV administration to a concentration not exceeding 4 mg/mL.** A dilution of 4 mg/mL may be prepared by adding 4 mL of the 10-mg/mL concentration to 6 mL D<sub>5</sub>W. After dilution the drug is stable at room temperature for 24 hours. Both forms should be stored at room temperature and protected from light.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, amphotericin B, aztreonam, cefepime, ceftazidime, ceftriaxone, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, erythromycin lactobionate, fluconazole, gentamicin, heparin, imipenem, linezolid, lorazepam, metoclopramide, morphine, nafcillin, oxacillin, piperacillin, piperacillin-tazobactam, potassium chloride, ranitidine, remifentanyl, tobramycin, trimethoprim-sulfamethoxazole, and vancomycin.

**Incompatibility:** Blood products and albumin solutions. Meropenem.

### Selected References

- ◆ Havens PL, Mofenson LM, Committee on Pediatric AIDS: Evaluation and management of the infant exposed to HIV-1 in the United States. *Pediatrics* 2009;123:175-187.
- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. May 24, 2010. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
- ◆ Capparelli EV, Mirochnick MH, Danker WM: Pharmacokinetics and tolerance of zidovudine in preterm infants. *J Pediatr* 2003;142:47-52.
- ◆ Alimenti A, Burdge DR, Ogilvie GS, et al: Lactic acidemia in human immunodeficiency virus-uninfected infants exposed to antiretroviral therapy. *Pediatr Infect Dis J* 2003;22:782-8.
- ◆ Mirochnick M, Capparelli E, Conner J: Pharmacokinetics of zidovudine in infants: A population analysis across studies. *Clin Pharmacol Ther* 1999;66:16-24.
- ◆ Acosta EP, Page LM, Fletcher CV: Clinical pharmacokinetics of zidovudine. *Drugs* 1996;30:251.
- ◆ Connor EM, Sperling RS, Gelber R, et al: Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173.
- ◆ Product Information, GlaxoSmithKline, 2006.

Compatibilities and References updated 7/2009

Adverse Effects/Precautions updated 1/2009





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# BIOLOGICALS

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Recommended Childhood Immunization Schedule United States, 2011

Vaccine	Age	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months
Hepatitis B <sup>1</sup>		HepB	HepB						
Rotavirus <sup>2</sup>				RV	RV	RV <sup>2</sup>			
Diphtheria, Tetanus, Pertussis <sup>3</sup>				DTaP	DTaP	DTaP	see footnote <sup>3</sup>		DTaP
<i>Haemophilus influenzae</i> type b <sup>4</sup>				Hib	Hib	Hib <sup>4</sup>	Hib		
Pneumococcal <sup>5</sup>				PCV	PCV	PCV	PCV		
Inactivated Poliovirus <sup>6</sup>				IPV	IPV			IPV	
Influenza <sup>7</sup>							Influenza (Yearly)		
Measles, Mumps, Rubella <sup>8</sup>								MMR	
Varicella <sup>9</sup>								Varicella	
Hepatitis A <sup>10</sup>								HepA (2 doses)	

■ Range of recommended ages

Approved by the Advisory Committee on Immunization Practices [www.cdc.gov/nip/acip](http://www.cdc.gov/nip/acip), the American Academy of Pediatrics [www.aap.org](http://www.aap.org) and the American Academy of Family Physicians [www.aafp.org](http://www.aafp.org).  
When using licensed combination vaccines, providers should consult the respective ACIP statement for detailed recommendations.

3. **Hepatitis B vaccine (HepB).** (Minimum age: birth)
 

At birth:

  - Administer monovalent HepB to all newborns before hospital discharge.
  - If mother is hepatitis B surface antigen (HBsAg)-positive, administer HepB and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
  - If mother's HBsAg status is unknown, administer HepB within 12 hours of birth. Determine mother's HBsAg status as soon as possible and if HBsAg-positive, administer HBIG (no later than age 1 week).

Doses following the birth dose:

  - The second dose should be administered at age 1–2 months. Monovalent HepB should be used for doses administered before age 6 weeks.
  - Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of at least 3 doses of the HepB series, at age 9–18 months (generally at the next well-child visit).
  - Administration of 4 doses of HepB to infants is permissible when a combination vaccine containing HepB is administered after the birth dose.
  - Infants who did not receive a birth dose should receive 3 doses of HepB on a schedule of 0, 1, and 6 months.
  - The final (3<sup>rd</sup> or 4<sup>th</sup>) dose in the HepB series should be administered no earlier than age 24 weeks.
2. **Rotavirus vaccine (RV).** (Minimum age: 6 weeks)
  - Administer the first dose at age 6–14 weeks (maximum age: 14 weeks 6 days). Vaccination should not be initiated for infants age 15 weeks or older.
  - The maximum age for the final dose in the series is 8 months 0 days.
  - If Rotarix® is given at ages 2 and 4 months, a dose at 6 months is not indicated.
3. **Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP).** (Minimum age: 6 weeks)
  - The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.
4. **Haemophilus influenzae type b conjugate vaccine (Hib).** (Minimum age: 6 weeks)
  - If PRP-OMP (PedvaxHib® or ComVax® [HepB-Hib]) is administered at ages 2 and 4 months, a dose at age 6 months is not indicated.
  - Hibrix® should not be used for doses at ages 2, 4 or 6 months for the primary series but can be used as the final dose in children 12 months through 4 years.
5. **Pneumococcal vaccine.** (Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPSV])
  - PCV is recommended for all children aged younger than 5 years. Administer 1 dose of PCV to all healthy children aged 24–59 months who are not completely vaccinated for their age.
  - A PCV series begun with 7-valent PCV (PCV7) should be completed with 13-valent PCV (PCV13).
  - A single supplemental dose of PCV13 is recommended for all children aged 14 through 59 months who have received an age-appropriate series of PCV7.
  - A single supplemental dose of PCV13 is recommended for all children aged 60 through 71 months with underlying medical conditions who have received an age-appropriate series of PCV7.
  - The supplemental dose of PCV13 should be administered at least 8 weeks after the previous dose of PCV7.
  - Administer PPSV at least 8 weeks after last dose of PCV to children aged  $\geq 2$  years with certain underlying medical conditions, including cochlear implant.
6. **Inactivated poliovirus vaccine (IPV).** (Minimum age: 6 weeks)
  - If 4 or more doses are administered prior to age 4 years, an additional dose should be administered at age 4 through 6 years.
  - The final dose in the series should be administered on or after the fourth birthday and at least 6 months following the previous dose.
7. **Influenza vaccine.** (Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 2 years for live, attenuated influenza vaccine [LAIV])
  - For healthy children aged 2 years and older (ie, those who do not have underlying medical conditions that predispose them to influenza complications), either LAIV or TIV may be used, except LAIV should not be given to children aged 2 through 4 years who have had wheezing in the past 12 months.
  - Administer 2 doses (separated by at least 4 weeks) to children aged 6 months through 8 years who are receiving seasonal influenza vaccine for the first time or who were vaccinated for the first time during the previous influenza season but only received 1 dose.
  - Children aged 6 months through 8 years who received no doses of monovalent 2009 H1N1 vaccine should receive 2 doses of 2010–2011 seasonal influenza vaccine.
8. **Measles, mumps, and rubella vaccine (MMR).** (Minimum age: 12 months)
9. **Varicella vaccine.** (Minimum age: 12 months)
10. **Hepatitis A vaccine (HepA).** (Minimum age: 12 months)

**(Diphtheria and tetanus toxoids for pediatric use)****Dose & Administration**

0.5 mL IM in the anterolateral thigh. Immunize premature infants according to their postnatal age. Please refer to most recent AAP/ACIP immunization schedule.

**When giving multiple vaccines, use a separate syringe for each and give at different sites.** Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

**Uses**

Immunoprophylaxis against diphtheria and tetanus for infants who have a contraindication for pertussis vaccine.

**Monitoring**

Observe injection site for erythema, induration (common), palpable nodule (uncommon), or sterile abscess (rare). Fever (common) may be treated with acetaminophen. Other common, self-limited, systemic effects are drowsiness, fretfulness, and anorexia. Rare anaphylactic reactions (i.e. hives, swelling of the mouth, hypotension, breathing difficulty, and shock) have been reported.

**Adverse Effects/Precautions**

Infants with stable neurologic conditions, including well-controlled seizures, may be vaccinated. Infants who have had prior seizures are at increased risk for seizures following DT vaccination; acetaminophen should be used to prevent postvaccination fever.

**Pharmacology**

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. DT vaccine is an aluminum-salt-adsorbed preparation.

**Special Considerations/Preparation**

DT vaccine (for pediatric use) is available as 0.5-mL single-dose vials. Store refrigerated. Do not freeze. Shake vial well before withdrawing each dose. Do not use if product contains clumps that cannot be resuspended with vigorous shaking. Normal appearance is a turbid whitish suspension.

**Selected References**

- ◆ American Academy of Pediatrics. Tetanus. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, ed. 2009 *Red Book: Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 68-70.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Product Information, Sanofi Pasteur, 2005

References updated 7/2009



(Diphtheria and tetanus toxoids and  
acellular pertussis vaccine adsorbed)

## BIOLOGICALS

**Dose & Administration**

0.5 mL IM in the anterolateral thigh. Shake vial vigorously before withdrawing each dose. Immunize premature infants according to their postnatal age. Please refer to the most recent AAP/ACIP immunization schedule.

**When giving multiple vaccines, use a separate syringe for each and give at different sites.** Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

**Uses**

Preferred immunoprophylaxis against diphtheria, tetanus, and pertussis.

**Monitoring**

Minor reactions, such as drowsiness, irritability, fever, anorexia, and pain/erythema/induration at the injection site are similar to those observed with DTwP vaccine, but are significantly less frequent. Moderate to severe reactions are also less frequent. Refer to Precautions section for more information.

**Adverse Effects/Precautions**

Those infants with stable neurologic conditions, including well-controlled seizures, may be vaccinated. Infants who have had prior seizures are at increased risk for seizures following DTP vaccination; acetaminophen should be used to prevent postvaccination fever.

**Precautions to further DTaP vaccination** (the benefits of administering DTaP may exceed risks in areas with a high incidence of pertussis; otherwise administer DT vaccine):

- 1) Temperature of  $\leq 40.5^{\circ}\text{C}$  ( $105^{\circ}\text{F}$ ) within 48 hours with no other cause.  
(Frequency approximately 1 child out of 16,000)
- 2) Hypotonic-hyporesponsive collapse or shock-like state within 48 hours.  
(Frequency approximately 1 child out of 14,000)
- 3) Inconsolable crying ( $\leq 3$  hours) occurring within 48 hours.  
(Frequency up to approximately 1 child out of 1,000)
- 4) Convulsions with or without fever occurring within 3 days.  
(Frequency approximately 1 child out of 14,000)

**Contraindications to further DTaP vaccination:** In children who develop encephalopathy within 7 days following any DTP vaccination, DT vaccine should be substituted for the remaining doses. In children who develop an immediate anaphylactic reaction, further immunization with any of the three antigens should be deferred. In children with a progressive neurologic disorder, it is prudent to delay the initial dose of DTaP vaccine until further observation and study have clarified their neurologic status and the effect of treatment.

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### Pharmacology

DTaP vaccines are aluminum-salt-adsorbed preparations. All acellular pertussis vaccines contain inactivated pertussis toxoid, but vary in the inclusion and concentration of four other pertussis antigens. Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. Daptacel®, Infanrix® and Tripedia® are thimerosal-free. Each dose of Daptacel® contains 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, 5 mcg fimbriae types 2 and 3, 5 mcg FHA, and 3 mcg pertactin, with 3.3 mg 2-phenoxyethanol as a preservative. Each dose of Infanrix® contains 25 Lf diphtheria toxoid, 10 Lf tetanus toxoid, 25 mcg inactivated toxin, 25 mcg FHA, and 8 mcg pertactin, with 2.5 mg 2-phenoxyethanol as a preservative. Each dose of Tripedia® contains 6.7 Lf diphtheria toxoid, 5 Lf tetanus toxoid, 23.4 mcg inactivated toxin, and 23.4 mcg FHA.

### Special Considerations/Preparation

FDA-licensed DTaP vaccines as of March 2008: Infanrix® (GlaxoSmithKline), available in single-dose vials and single-dose prefilled syringes, Daptacel® (Sanofi Pasteur), available in single-dose vials and multi-dose vials, and Tripedia® (Sanofi Pasteur), available in single-dose vials. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.** SHAKE VIAL WELL before withdrawing dose. Do not use if product contains clumps that cannot be resuspended with vigorous shaking. Normal appearance is a homogeneous (Tripedia® and Daptacel®) or turbid (Infanrix®) white suspension.

### Selected References

- ◆ American Academy of Pediatrics. Pertussis. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 510-513.
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases : Acellular pertussis vaccine: recommendations for use as the initial series in infants and children. *Pediatrics* 1997;99:282.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Product information, GlaxoSmithKline, 2007.
- ◆ Product information, Sanofi Pasteur, 2005, 2008.

Adverse Effects/Precautions and References updated 7/2009



[Diphtheria and tetanus toxoids and acellular pertussis adsorbed, Hepatitis B (recombinant) and inactivated poliovirus vaccine combined]

### Dose & Administration

0.5 mL IM in the anterolateral thigh. Shake vial vigorously before withdrawing dose.

PEDIARIX® should not be administered to any infant before the age of 6 weeks. Only monovalent hepatitis B vaccine can be used for the birth dose.

Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; however, inadequate seroconversion against hepatitis B may occur in chronically ill premature infants.

### Uses

Immunoprophylaxis against diphtheria, tetanus, pertussis, hepatitis B, and polio. Using PEDIARIX® to complete the hepatitis B vaccination series in infants who were born of HBsAg-positive mothers and who received monovalent Hepatitis B vaccine (Recombinant) has not been studied.

### Monitoring

Cardiorespiratory monitoring and pulse oximetry are recommended for premature infants who remain hospitalized at the time of vaccination.

### Adverse Effects/Precautions

Fever is more common (≈20%) after PEDIARIX® than with the individual component vaccines administered separately. Other local and systemic adverse events occur at similar rates. Apnea, bradycardia, and desaturation events are common in premature infants for 48 hours after vaccination.

### Pharmacology

Each dose of PEDIARIX® contains the type and amount of diphtheria and tetanus toxoids and pertussis antigens as INFANRIX®, and hepatitis B virus antigens as Engerix-B®. The poliovirus component of DTaP-HepB-IPV contains the same strains and quantity of inactivated poliovirus Types 1, 2, and 3 as IPV from a different manufacturer (IPOL®, Sanofi Pasteur). The immunologic responses following 3 doses of DTaP-HepB-IPV were generally similar to those following 3 doses of the individual vaccines administered separately.

### Special Considerations/Preparation

PEDIARIX® is supplied as a turbid white suspension in single dose (0.5 mL) vials, and in disposable prefilled Tip-Lock® syringes. Shake well prior to administration. Do not use if resuspension does not occur after vigorous shaking. Store refrigerated at 2° to 8°C (36°F to 46°F). **Do not freeze.** Discard if the vaccine has been frozen.

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**Selected References**

- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Centers for Disease Control and Prevention: FDA licensure of diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and poliovirus vaccine combined, (PEDIARIX<sup>TM</sup>) for use in infants. *MMWR* 2003;52(RR-10):202-203.
- ◆ Pfister RE, Aeschbach V, Niksic-Stuber V, et al: Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* 2004;145:58-66.
- ◆ Product information, GlaxoSmithKline Biologicals, 2007.

Monitoring updated 3/2005

**Dose & Administration**

200 to 400 units/kg/dose, 3 to 5 times per week, for 2 to 6 weeks.  
Total dose **per week** is 600 to 1400 units per kg.

**Short course:** 300 units/kg per dose daily for 10 days.

Administer subQ, or IV over at least 4 hours (even continuously in TPN).

Supplemental iron therapy should be initiated concurrently.

**Uses**

To stimulate erythropoiesis and decrease the need for erythrocyte transfusions in high-risk preterm infants. Those most likely to benefit are infants with birth weights less than 800 g and phlebotomy losses greater than 30 mL/kg.

**Monitoring**

Weekly CBC to check for neutropenia and monitor RBC response.

**Adverse Effects/Precautions**

The only adverse effect in premature neonates is neutropenia, which occurs rarely and resolves with discontinuation of the drug.

**Black Box Warning**

According to the manufacturer's black box warning, (adult) patients with renal failure experienced greater risks for death and serious cardiovascular events when higher hemoglobin levels were achieved. It is recommended that (adult) patients with renal failure achieve and maintain hemoglobin levels of 10 to 12 g/dL. The relevance of this finding to the neonatal population is unknown.

**Pharmacology**

Epoetin alfa is a 165-amino acid glycoprotein manufactured by recombinant DNA technology that has the same biological effects as endogenous erythropoietin. It acts on mature erythroid progenitors, CFU-E, by binding to cell surface receptors and stimulating differentiation and cell division. Noticeable effects on hematocrit and reticulocyte counts occur within 2 weeks. Adequate iron and protein intake is necessary for epoetin to be effective (additional Vitamin E intake may be necessary as well). Subcutaneously administered drug appears to be pharmacodynamically as effective as IV, despite only 40% bioavailability. Half-life of r-HuEPO in preterm infants is approximately 12 hours. Doses reported in the literature are all stated as units/kg **per week**. Efficacy may be dose dependent in the range of 500 to 1500 units/kg per week (see meta-analysis by Garcia et al), but no differences were observed in the randomized trial by Maier et al.

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### Special Considerations/Preparation

Available in preservative-free, single-use, 1-mL vials containing 2000, 3000, 4000, 10,000, or 40,000 units formulated in an isotonic, sodium chloride/sodium citrate buffered solution with 2.5 mg human albumin. Store refrigerated at 2 to 8 degrees C (36 to 46 degrees F). **Do not freeze or shake.** Undiluted epoetin is stable in plastic syringes for 2 weeks. For IV infusion, dilute epoetin in 2 mL of solutions containing at least 0.05% protein and infuse over 4 hours. These dilutions are stable for 24 hours. Product support for use in neonates is handled by Ortho Biotech, Inc. (Procrit®). Multidose 1-mL (20,000 units/mL) and 2-mL (10,000 units/mL) vials are also available from both Ortho Biotech (Procrit®) and Amgen (Epogen®) containing 1% (10 mg/mL) benzyl alcohol solution with 2.5-mg albumin per mL. Discard multidose vials 21 days after initial entry.

### Selected References

- ◆ Reiter PD, Rosenberg AA, Valuck R, Novak K: Effect of short-term erythropoietin therapy in anemic premature infants. *J Perinatol* 2005;25:125-129.
- ◆ Ohls R: Human recombinant erythropoietin in the prevention and treatment of anemia of prematurity. *Paediatr Drugs* 2002;4:111-121.
- ◆ Garcia MG, Hutson AD, Christensen RD: Effect of recombinant erythropoietin on "late" transfusions in the neonatal intensive care unit: A meta-analysis. *J Perinatol* 2002;22:108-111.
- ◆ Donato H, Vain N, Rendo P, et al: Effect of early versus late administration of human recombinant human erythropoietin on transfusion requirements in premature infants: Results of a randomized, placebo-controlled, multicenter trial. *Pediatrics* 2000;105:1066.
- ◆ Maier RF, Obladen M, Kattner E, et al: High- versus low-dose erythropoietin in extremely low birth weight infants. *J Pediatr* 1998;132:866-870.
- ◆ Ohls RK, Christensen RD: Stability of recombinant human epoetin alfa in commonly used neonatal intravenous solutions. *Ann Pharmacother* 1996;30:466.
- ◆ Shannon KM, Keith JF, Mentzer WC, et al: Recombinant human erythropoietin stimulates erythropoiesis and reduces erythrocyte transfusions in very low birth weight preterm infants. *Pediatrics* 1995;95:1.
- ◆ Ohls RK, Osborne KA, Christensen RD: Efficacy and cost analysis of treating very low birth weight infants with erythropoietin during their first two weeks of life: A randomized placebo controlled trial. *J Pediatr* 1995;126:421.
- ◆ Meyer MP, Meyer JH, Commerford A, et al: Recombinant erythropoietin in the treatment of the anemia of prematurity: Results of a double-blind, placebo-controlled study. *Pediatrics* 1994;93:918.
- ◆ Product Information, Amgen, 2009.
- ◆ Product Information, Ortho Biotech, 2009.

Special Considerations and References updated 12/2010

Adverse Effects/Precautions updated 1/2009

Dose updated 3/2006

**Dose & Administration**

0.5 mL IM in the anterolateral thigh. Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; however, inadequate seroconversion may occur in chronically ill premature infants.

For HbOC and PRP-T, second and third doses are given at 2-month intervals, followed by a fourth dose given at age 15 months.

For PRP-OMP, only the second dose is given after a 2-month interval; the third dose is given at age 15 months.

**When giving multiple vaccines, use a separate syringe for each and give at different sites.** Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

**Uses**

Immunoprophylaxis against invasive disease caused by *Haemophilus influenzae* type b.

**Monitoring**

Observe injection site for local reactions.

**Adverse Effects/Precautions**

Soreness at the injection site with local erythema, swelling, tenderness, and fever.

**Pharmacology**

Three conjugate vaccines are currently approved for use in infants older than 2 months of age. These vaccines are derived from *H influenzae* type b capsular polysaccharide, polyribosylribitol phosphate (PRP), which is linked to a T-cell-dependent protein antigen to enhance immunogenicity.

**Special Considerations/Preparation**

HibTITER® is a clear, colorless solution supplied in single-dose (preservative-free) vials. Discard if discolored or turbid. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

ActHIB® is supplied as lyophilized powder. Store the lyophilized vaccine and diluent refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.** Reconstitute using only the 0.4% saline diluent provided in single-use 0.6-mL vials and use immediately. Reconstituted vaccine is a clear, colorless solution.

Liquid PedvaxHIB® is supplied in single-dose vials. It is a slightly opaque white suspension. Shake well before withdrawal and use. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

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## Products

Manufacturer	Abbreviation	Trade Name	Carrier Protein
Wyeth-Lederle Pharmaceuticals	HbOC	HibTITER®	CRM197 (a nontoxic mutant diphtheria toxin)
Sanofi Pasteur	PRP-T	ActHIB®	Tetanus toxoid
Merck & Co, Inc	PRP-OMP Liquid	PedvaxHIB®	OMP (an outer membrane protein complex of N meningitidis)

## Selected References

- ◆ American Academy of Pediatrics. *Haemophilus Influenzae* Infections. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. Red Book: 2009 Report of the Committee on Infectious Diseases. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 317-321.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Washburn LK, O'Shea TM, Gillis DC, et al: Response to *Haemophilus influenzae* type b conjugate vaccine in chronically ill premature infants. *J Pediatr* 1993;123:791.
- ◆ Product information, Wyeth-Lederle Pharmaceuticals, 2007.
- ◆ Product information, Sanofi Pasteur, 2005.
- ◆ Product information, Merck & Co, 2004.

References updated 7/2009

**Dose & Administration**

0.5 mL IM in the anterolateral thigh.

**Term and preterm newborns born to HBsAg-positive mother:** Give within 12 hours of birth.

**Term and preterm newborns born to HBsAg status unknown mother with BW greater than or equal to 2000 g:** Give as soon as it is determined that the mother is HBsAg-positive, within 7 days of birth.

**Preterm newborns born to HBsAg status unknown mother with BW less than 2000 g:** If mother's status unavailable, give within 12 hours of birth.

**When given at the same time as the first dose of hepatitis B vaccine,** use a separate syringe and a different site. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

**Uses**

Passive immunization of newborns whose mothers have acute hepatitis B infection at the time of delivery, or who are HBsAg-positive. Infants born to mothers who are HBeAg-positive have the highest risk.

**Monitoring**

No specific monitoring required.

**Adverse Effects/Precautions**

Local pain and tenderness may occur at the injection site.

**Do not administer IV** because of the risk of serious systemic reactions. Serious complications of IM injections are rare. Universal precautions should be used with neonates born to HBsAg-positive mothers until they have been bathed carefully to remove maternal blood and secretions.

**Pharmacology**

Hepatitis B Immune Globulin (human) is a hyperimmune globulin solution prepared from pooled plasma of individuals with high titers of antibody to hepatitis B surface antigen (anti-HBsAg). All donors are HBsAg-negative and HIV-antibody negative. Nabi-HB™ (Nabi) and BayHep B™ (Bayer) are solvent detergent treated and thimerosal free hepatitis B immune globulin preparations.

**Special Considerations/Preparation**

Refrigerate. Supplied in 1-mL and 5-mL single-dose vials and 0.5-mL unit-dose syringes.

**Selected References**

- ♦ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 343-350.
- ♦ Crumpacker CS: Hepatitis, in Remington JS, Klein JO (eds): *Infectious Diseases of the Fetus and Newborn Infant*, ed 5. Philadelphia: WB Saunders Co, 2001, pp 932-33.
- ♦ Product Information, Cangene, 2006.

References updated 7/2009

Updated 3/2008





**Dose & Administration**

Engerix-B® 10 mcg (0.5 mL) or Recombivax HB® 5 mcg (0.5 mL) IM.

**Maternal HBsAg-Positive:** Administer first dose before 12 hours of age regardless of birth weight (administer HBIG also). Infants with BW less than 2000 g should receive 3 additional vaccine doses, beginning at 1 to 2 months of age.

**Maternal HBsAg Unknown:** Administer first dose before 12 hours of age regardless of birth weight. If BW less than 2000 g, administer HBIG if mother tests HBsAg positive or if mother's HBsAg result is not available within 12 hours of age. Administer HBIG to newborns with BW greater than or equal to 2000 g within 7 days of birth if the mother tests HBsAg positive.

**Maternal HBsAg Negative:** Administer first dose shortly after birth, before hospital discharge. If BW less than 2000 g and medically stable, administer first dose at 30 days of chronologic age or at time of hospital discharge if before 30 days of chronologic age.

Please refer to the most recent AAP/ACIP immunization schedule for subsequent doses. Engerix-B® also has an alternative four-dose schedule: Birth, 1, 2, and 12 to 18 months of age.

**Uses**

Immunoprophylaxis against hepatitis B. Safe for use in infants born to HIV-positive mothers, although it may be less effective.

**Monitoring**

Testing for immunity 3 months after completion of the vaccination series is recommended for infants born to HBsAg-positive mothers and, perhaps, for premature infants who received an early first dose.

**Adverse Effects/Precautions**

The only common side effect is soreness at the injection site. Fever greater than 37.7 °C occurs in 1% to 6%.

**Pharmacology**

Recombinant hepatitis B vaccines are produced by *Saccharomyces cerevisiae* (common baker's yeast) that has been genetically modified to synthesize HBsAg. Both vaccines are inactivated (noninfective) products that contain HBsAg protein adsorbed to aluminum hydroxide, and may be interchanged with comparable efficacy.

**Special Considerations/Preparation**

Recombivax HB® for infant use is supplied in 0.5 mL single-dose vials and single-dose prefilled syringes containing 5 mcg. Engerix-B® is supplied in 0.5 mL single-dose vials and 0.5 mL single-dose prefilled disposable syringes containing 10 mcg per 0.5 mL. Preservative free. The vaccine should be used as supplied; do not dilute. **Shake well before withdrawal and use.** Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze** -destroys potency.

*continued...*

**Selected References**

- ◆ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 343-350.
- ◆ Centers for Disease Control and Prevention: A comprehensive immunization strategy to eliminate transmission of hepatitis B virus in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children and adolescents. *MMWR Recomm Rep* 2005;54 (RR-16):1-23.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Saari TN, Committee on Infectious Diseases: Immunization of preterm and low birth weight infants. *Pediatrics* 2003;112:193-98.
- ◆ Product Information, Merck and Company, 2007
- ◆ Product Information, GlaxoSmithKline, 2006

Dose & Administration and References updated 7/2009

Updated 3/2008

## Hib Conjugate/Hepatitis B Combination Vaccine

### BIOLOGICALS

#### Dose & Administration

0.5 mL IM in the anterolateral thigh.

Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; some data, however, suggest delaying the first dose in chronically ill premature infants due to inadequate seroconversion against *H influenzae*.

**When giving multiple vaccines, use a separate syringe for each and give at different sites.** Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

#### Uses

COMVAX® is indicated for vaccination against invasive disease caused by *Haemophilus influenzae* type b and against infection caused by all known subtypes of hepatitis B virus in infants 6 weeks to 15 months of age born to HBsAg-negative mothers. COMVAX® should not be used in infants younger than 6 weeks of age.

#### Monitoring

Observe injection site for local reactions.

#### Adverse Effects/Precautions

Local pain and tenderness may occur at the injection site.

#### Pharmacology

COMVAX® (preservative-free) combines the antigenic components of Recombivax HB® and PedvaxHIB®. Each 0.5 mL dose contains 5 mcg HBsAg and 7.5 mcg *Haemophilus b* -PRP.

#### Special Considerations/Preparation

Supplied in 0.5-mL single-dose vial. Store refrigerated. **Do not freeze.**

#### Selected References

- ◆ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 343-345.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ Product information, Merck & Co, 2004.

References updated 7/2009



## Intravenous Immune Globulin (Human)

### Dose & Administration

Usual dosage: 500 to 750 mg/kg per dose over 2 to 6 hours.

For neonatal alloimmune thrombocytopenia, doses have ranged from 400 mg/kg to 1 gram/kg.

Most studies have used a single dose, although additional doses have been given at 24 hour intervals.

### IVIG Product-Specific Administration

Brand	Infusion Rate	Infusion Rate in Renal Disease/Thrombotic Complications	Filter/Flushing Compatibility
Carimune(R) NF (CSL Behring AG)	Use the 3% sol'n for the first infusion at initial rate of 0.5 mg/kg/min; increase to 1 mg/kg/min after 30 minutes; up gradually to a maximum of 3 mg/kg/min.	Maximum rate less than 2 mg/kg/min.	Optional (15 micron or higher)/D5W or NS
Febogamma(R) 5% and 10% DIF (Grifols)	Initial, 0.01 mL/kg/min; increase gradually during the first 30 minutes to a maximum of 0.1 mL/kg/min for 5% sol'n and 0.08 mL/kg/min for 10% sol'n.	Minimum rate practicable.	5%, yes; 15 to 20 microns; 10%, not available/Not available
GAMMAGARD Liquid 10% (Baxter)	Initial, 0.5 mL/kg/hr; increase every 30 minutes to a rate of 5 mL/kg/hr.	Maximum rate less than 2 mL/kg/hr.	Optional/D5W
GAMMAGARD S/D (Baxter)	Initial, infuse 5% sol'n at rate of 0.5 mL/kg/hr; increase gradually to 4 mL/kg/hr if tolerated; subsequent infusion of 10% sol'n starts at 0.5 mL/kg/hr, increase to 8 mL/kg/hr as tolerated. Antecubital veins for 10% sol'n.	Maximum rate less than 4 mL/kg/hr of 5% sol'n, or less than 2 mL/kg/hr of a 10% sol'n.	Yes/Not available

*continued...*

## IVIG Product-Specific Administration (continued)

Brand	Infusion Rate	Infusion Rate in Renal Disease/Thrombotic Complications	Filter/Flushing Compatibility
Gammaplex(R) 5% (Bio Products Lab)	Initial, 0.01 mL/kg/min for 15 minutes; increase every 15 minutes to 0.08 mL/kg/min.	Minimum rate practicable.	Yes (15 to 20 micron)/Not available
Gammar(R)-PIV (ZLB Behring)	With the reconstituted sol'n of 50 mg/mL, start at 0.01 mL/kg/min; increase to 0.02 mL/kg/min after 15 to 30 minutes; increase gradually up to a maximum of 0.06 mL/kg/min.	Do not exceed 0.02 mL/kg/min (1 mg/kg/min) (Epstein & Zoon, 1999).	Optional (15 micron or higher)/D5W or NS
Gamunex(R) 10% (Talecris)	Initial, 0.01 mL/kg/min (1 mg/kg/min) for the first 30 minutes and gradually increase up to 0.08 mL/kg/min (8 mg/kg/min) if tolerated.	Minimum rate practicable.	No/D5W
Polygam(R) S/D (Baxter)	Initial, infuse 5% sol'n at rate of 0.5 mL/kg/hr; increase gradually to 4 mL/kg/hr if tolerated; subsequent infusion of 10% sol'n starts at 0.5 mL/kg/hr, increase to 8 mL/kg/hr as tolerated. Antecubital veins for 10% sol'n.	Maximum rate less than 4 mL/kg/hr for a 5% sol'n, or less than 2 mL/kg/hr for a 10% sol'n.	Yes/Not available
Privigen(R) 10% (CSL Behring AG)	Initial, 0.005 mL/kg/min and increase gradually to 0.04 mL/kg/min (maximum 0.08 mL/kg/min).	Minimum rate practicable.	No/D5W or NS

sol'n = solution

continued...

## Intravenous Immune Globulin (Human)

### BIOLOGICALS

#### Uses

Adjuvant treatment of fulminant neonatal sepsis, hemolytic jaundice, and neonatal alloimmune thrombocytopenia.

#### Monitoring

Frequent monitoring of heart rate and blood pressure. Check IV site for signs of phlebitis.

#### Adverse Effects/Precautions

##### Black Box Warning

According to the manufacturer's black box warning, immune globulin intravenous (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Use caution in patients predisposed to acute renal failure and administer at the minimum concentration available and the minimum rate of infusion practicable in such patients. Higher rates of renal failure were associated with IGIV products containing sucrose.

Rare cases of hypoglycemia, transient tachycardia, and hypotension that resolved after stopping the infusion have been reported. The risk of necrotizing enterocolitis may be increased in term and late preterm infants treated for isoimmune hemolytic jaundice. Animal studies have demonstrated reticuloendothelial system blockade when higher doses (greater than 1 g/kg) have been used. All donor units are nonreactive to HBsAg and HIV. The manufacturing process of these products now includes a solvent/detergent treatment to inactivate hepatitis C and other membrane-enveloped viruses.

#### Pharmacology

IVIG is a plasma-derived, concentrated form of IgG antibodies present in the donor population. Significant lot-to-lot variation of specific antibodies may occur with all products. No significant differences in clinical outcomes using the different products have been seen. All preparations are reported to contain more than 92% IgG monomers and a normal distribution of IgG subclasses. Total IgG titers in treated, septic neonates remain elevated for approximately 10 days.

#### Special Considerations/Preparation

\*Reconstitute lyophilized products with supplied diluent. **DO NOT SHAKE** vials; swirl gently to mix. All products are preservative free. **DO NOT FREEZE** ; products that have been frozen should not be used. Shelf life varies, but is at least 2 years, when stored properly. **Do not mix IVIG products from different manufacturers.\***

*continued...*

## IVIG Preparations

Brand	Form	Sugar	Preparation/Storage/ Stability
Carimune NF (CSL Behring AG)	3, 6, and 12 g lyophilized vials	1.67 g sucrose/g IVIG	Store at room temperature. Use immediately after reconstitution if prepared outside of sterile laminar air flow hood. Solution is stable for 24 hours with aseptic technique and continuous refrigeration. Compatible with NS and D5W.
Flebogamma 5% and 10% DIF (Grifols)	5% and 10% ready-for-use solution	50 mg/mL D- sorbitol	Store at room temperature or refrigerated. Use immediately once vial has been entered and discard any unused portion. Not recommended to be mixed with any other IV solutions or medications.
Gammagard Liquid 10% (Baxter)	10% ready- for-use solution	None (glycine stabilized)	Store at room temperature or refrigerated. Should be at room temperature during administration. Compatible with D5W (not compatible with NS).
Gammagard S/D (Baxter)	2.5, 5, and 10 g lyophilized vials	2% glucose	Store at room temperature. Use immediately (no more than 2 hours after reconstitution if prepared outside of sterile laminar air flow hood). Stable for 24 hours with aseptic technique and refrigeration. Do not mix with other IV solutions or medications.
Gammaplex 5% (Bio Products Lab)	5% ready-for- use solution	50 mg/mL D- sorbitol	Room temperature or refrigerated. Use immediately once vial has been entered; discard unused portion. Infuse within 2 hours if vials are pooled for large doses. Vials stopper top contain 13% natural rubber. Do not mix with other IV fluids or medications.

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# Intravenous Immune Globulin (Human)

## IVIG Preparations (continued)

Brand	Form	Sugar	Preparation/Storage/Stability
Gammar-P IV (ZLB Behring)	5 and 10 g lyophilized vials	5% sucrose	Store at room temperature. Infusion must be started within 3 hours of reconstitution. Compatible with NS and D5W.
Gammunex 10% (Talecris)	10% ready-for-use solution	None (glycine stabilized)	Room temperature or refrigerated. Use immediately once vial has been entered; discard unused portion. Vials pooled under aseptic conditions must be used within 8 hours. Packaging components are latex free. Compatible with D5W, but not with NS.
Panoglobulin NF (ZLB Bioplasma AG)	1, 3, 6, and 12 g lyophilized vials	1.67 g sucrose/g IVIG	Store at room temperature. Administer immediately after reconstitution if prepared outside sterile laminar air flow hood. Solution is stable for 24 hours with aseptic conditions and continuous refrigeration. Compatible with NS and D5W.
Polygam S/D (Baxter)	2.5, 5, and 10 g lyophilized vials	2% glucose	Store at room temperature. Use immediately (no more than 2 hours after reconstitution if prepared outside of sterile laminar air flow hood). Stable for 24 hours with aseptic technique and refrigeration. Compatible with D5W and NS.
Privigen 10% (CSL Behring AG)	10% ready-for-use solution	None (L-proline stabilized)	Store at room temperature. Use immediately once vial has been entered and discard any unused portion. Contents of vials pooled under aseptic conditions must be used within 8 hours. Packaging components are latex free. Compatible with D5W.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>15</sub>W, and Dex/AA.

**Terminal Injection Site Compatibility:** Fluconazole.

*continued...*

## Selected References

- ◆ Figueras-Aloy J, Rodriguez-Miguel JM, Iriondo-Sanz M, et al: Intravenous immunoglobulin and necrotizing enterocolitis in newborns with hemolytic disease. *Pediatrics* 2010;125:139-144.
- ◆ Kreyman KG, de Heer C, Nierhaus A, Kluge S: Use of polyclonal immunoglobulins as adjunctive therapy for sepsis or septic shock. *Crit Care Med* 2007;35:2677-2685.
- ◆ Sandberg K, Fasth A, Berger A, et al: Preterm infants with low immunoglobulin G levels have increased risk for neonatal sepsis but do not benefit from prophylactic immunoglobulin G. *J Pediatr* 2000;137:623-628.
- ◆ Jenson HB, Pollock BH: Meta-analyses of the effectiveness of intravenous immune globulin for prevention and treatment of neonatal sepsis. *Pediatrics* 1997;99(2):e2.
- ◆ Blanchette VS, Rand ML: Platelet disorders in newborn infants: diagnosis and management. *Semin Perinatol* 1997;21:53-62.
- ◆ Weisman LE, Stoll BJ, Kueser TJ: Intravenous immunoglobulin therapy for early-onset sepsis in premature neonates. *J Pediatr* 1992;121:434.
- ◆ Christensen RD, Brown MS, Hall DC, et al: Effect on neutrophil kinetics and serum opsonic capacity of intravenous administration of immune globulin to neonates with clinical signs of early-onset sepsis. *J Pediatr* 1991;118:606.
- ◆ Figueras-Aloy J, Rodriguez-Miguel JM, Iriondo-Sanz M, et al: Intravenous immunoglobulin and necrotizing enterocolitis in newborns with hemolytic disease. *Pediatrics* 2010;125:136-141.
- ◆ Gottstein R, Cooke RWI: Systematic review of intravenous immunoglobulin in haemolytic disease of the newborn. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F6-F10.
- ◆ Tanyer G, Suklar Z, Dallar Y, et al: Multiple dose IVIG treatment of neonatal immune hemolytic jaundice. *J Trop Pediatr* 2001;47:50-53.

Preparation Chart and References updated 12/2010

Adverse Effects/Precautions and References updated 1/2010

**Dose & Administration**

15 mg/kg per dose IM, preferably in the anterolateral aspect of the thigh.

Repeat monthly during RSV season.

**Uses**

Immunoprophylaxis against severe RSV lower respiratory tract infections in high risk infants:

- ◆ up to 24 months of age, hemodynamically significant acyanotic and cyanotic congenital heart disease (maximum 5 doses),
- ◆ less than 24 months of age, chronic lung disease of prematurity (CLD) who have required medical therapy for CLD within 6 months before the start of the RSV season (maximum 5 doses),
- ◆ up to 12 months of age, born at 28 weeks gestation or earlier (maximum 5 doses),
- ◆ up to 6 months of age, born at 29 to 31 weeks, 6 days gestation (maximum 5 doses),
- ◆ less than 3 months of age, born between 32 to 34 weeks, 6 days gestation with at least 1 risk factor and born 3 months before or during RSV season (maximum 3 doses or stop therapy at 3 months of age),
- ◆ infants born before 35 weeks of gestation with congenital abnormalities of the airway or a neuromuscular disease that compromises handling of respiratory secretions (maximum 5 doses during first year of life).

Risk factors include child care attendance or a sibling less than 5 years of age.

Once an infant qualifies for initiation of prophylaxis, it should continue throughout the RSV season, with the exception of infants 32 to less than 35 weeks gestation. Palivizumab is not effective for treatment of established RSV disease.

**Monitoring**

Observe injection site for induration and swelling.

**Adverse Effects/Precautions**

In clinical trials, upper respiratory infection, otitis media, fever, and rhinitis occurred slightly more frequently in palivizumab recipients. Cyanosis and arrhythmia were also seen slightly more frequently in patients with CHD. There are rare reports (less than 1 per 100,000 patients) of anaphylaxis, and hypersensitivity reactions have been reported. Do not administer to patients with a history of a prior severe reaction.

**Pharmacology**

Synagis® is a humanized monoclonal antibody produced by recombinant DNA technology. This composite of human (95%) and murine (5%) antibody sequences inhibits RSV replication. The mean half-life of Synagis® is approximately 20 days. Adequate antibody titers are maintained in most infants for one month following a 15-mg/kg dose. Due to a faster metabolic rate, some hospitalized VLBW infants (less than 500 g) may not maintain optimal RSV titers for the entire initial month until after the second dose. Palivizumab does not interfere with the response to other vaccines and as such, they can be administered concurrently.

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**Special Considerations/Preparation**

Synagis® is supplied as 50-mg and 100-mg single-dose vials in ready-to-use, **NO RECONSTITUTION required**, liquid solution. Do not add any diluent to the liquid solution and use one dose per vial. Do not re-enter vial after initial withdrawal and discard any unused portions. Administer as soon as possible after withdrawal from the vial. **Do not FREEZE or SHAKE.** The liquid solution should be stored **refrigerated between 2 to 8°C (36 to 46°F)**. Synagis® contains no preservatives, thimerosal, or other mercury salts.

**Selected References**

- ◆ American Academy of Pediatrics. Respiratory Syncytial Virus (RSV) Infections. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28<sup>th</sup> ed. Elk Grove Village, IL: American Academy of Pediatrics 2009:562-569.
- ◆ Meissner HC, Long SS, Committee on Infectious Diseases and Committee on Fetus and Newborn: Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Policy Statement and Technical Report. *Pediatrics* 2003;122:1442-46 and 1447-52.
- ◆ Romero JR: Palivizumab prophylaxis of respiratory syncytial virus disease from 1998 to 2002: results from four years of palivizumab usage. *Pediatr Infect Dis J* 2003;22:546-54.
- ◆ The Impact-RSV Study Group: Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. *Pediatrics* 1998;102:531-537.
- ◆ Groothuis JR: Safety and tolerance of palivizumab administration in a large northern hemisphere trial. *Pediatr Infect Dis J* 2001;20:628-629.
- ◆ Wu S-Y, Bonaparte J, Pyati S: Palivizumab use in very premature infants in the neonatal intensive care unit. *Pediatrics* 2004;114:e554-e556.
- ◆ Product Information, MedImmune, 2009.

Uses and References updated 7/2009

## Pneumococcal 13-Valent Conjugate Vaccine (PCV13)

### Dose & Administration

0.5 mL IM; the usual vaccination schedule of pneumococcal 13-valent conjugate vaccine (PCV13) consists of 4 doses given at 2 months (as young as 6 weeks of age is acceptable), 4 months, 6 months, and 12 to 15 months of age. The recommended dosing interval is 4 to 8 weeks.

Administer IM in the anterolateral thigh. Do not inject IV, subQ, or intradermally.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

### Uses

Immunoprophylaxis against invasive disease caused by *S. pneumoniae* due to the 13 serotypes contained in the vaccine (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) and for prevention of otitis media caused by the 7 serotypes contained in the vaccine (4, 6B, 9V, 14, 18C, 19F, and 23F) in children 6 weeks to less than 59 months of age.

### Monitoring

Observe injection site for erythema, induration (common), palpable nodule (uncommon), or sterile abscess (rare).

### Adverse Effects/Precautions

**Contraindicated** in patients with a serious allergic reaction (eg, anaphylaxis) after a previous pneumococcal vaccine dose, or any diphtheria toxoid-containing vaccine.

Vaccination should be deferred in patients with moderate or severe acute illness, with or without fever. Immunocompromised patients may have a suboptimal response to the vaccine. Local injection site reactions (eg, erythema, induration, and tenderness) are common (greater than 20%) after each injection. Systemic reactions (eg, fever, irritability, decreased appetite, or decreased/increased sleep) are common (greater than 20%). Rare anaphylactic reactions (eg, hives, swelling of the mouth, hypotension, breathing difficulty, and shock) have been reported.

### Pharmacology

PCV13 contains the original 7 pneumococcal capsular polysaccharides found in PCV7 and 6 additional pneumococcal serotypes (1, 3, 5, 6A, 7F, and 19A), which have been attributed to 64% of invasive pneumococcal disease now occurring in US children younger than 5 years of age (the 7 original serotypes account for 83% of the disease in the US). PCV13 is a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F individually conjugated to diphtheria CRM197 protein. The increased antigenic load of PCV13 did not interfere with immune responses against other vaccines given concurrently nor did it increase vaccine reactogenicity during clinical trials. Each dose contains 0.125 mg aluminum as aluminum phosphate adjuvant.

*continued...*

**Special Considerations/Preparation**

Prevnar 13™ is supplied in 0.5-mL single-dose, latex-free, pre-filled syringes. Store refrigerated at 2 to 8 degrees C (36 to 46 degrees F). **Do not freeze; discard if frozen.** Shake vigorously prior to use. Vaccine should appear as a homogeneous white suspension; do not use if it cannot be resuspended. Do not mix with other vaccines.

**Selected References**

- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>.
- ◆ American Academy of Pediatrics (AAP): Policy statement recommendations for the prevention of streptococcus pneumonia infections in infants and children: use of 13-valent pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPSV23). *Pediatrics* 2010; 126: published online May 24, 2010.
- ◆ Bryant KA, Block SL, Baker SA, et al: Safety and immunogenicity of a 13-valent pneumococcal conjugate vaccine. *Pediatrics* 2010; 125:866-875.
- ◆ Centers for Disease Control and Prevention: Licensure of a 13-valent pneumococcal conjugate vaccine (PCV13) and recommendations for use among children - Advisory Committee on Immunization Practices (ACIP), 2010. *MMWR* 2010; 59(9):258-261.
- ◆ Centers for Disease Control and Prevention: Invasive pneumococcal disease in young children before licensure of 13-valent pneumococcal conjugate vaccine-United States, 2007. *MMWR* 2010; 59(9):253-257.
- ◆ Centers for Disease Control and Prevention: General recommendations on immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2006; 55(RR-15):1-48.
- ◆ Esposito S, Tansey S, Thompson A, et al: Safety and immunogenicity of 13-valent pneumococcal conjugate vaccine compared to 7-valent pneumococcal. *Clin Vaccine Immunol* 2010 April 28 [Epub ahead of print].
- ◆ Product information: Prevnar 13™ pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein), Wyeth Pharmaceuticals, 2010.
- ◆ Yeh, SH, Gurtman A, Hurley DC, et al: Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in infants and toddlers. *Pediatrics* 2010;16:e493-e505.

Added 12/2010

## Poliovirus Vaccine Enhanced-Inactivated

### Dose & Administration

0.5 mL injected **subcutaneously** in the midlateral thigh or IM in the anterolateral thigh. Immunize premature infants according to their postnatal age. Please refer to the most recent immunization schedule. **When giving multiple vaccines, use a separate syringe for each and give at different sites.** Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

### Uses

Inactivated poliovirus vaccine is now the only poliovirus vaccine available in the United States. Indications in other countries include hospitalized infants, and infants with contraindications for OPV (e.g. immunodeficiency, HIV-positive, those with immunodeficient contacts).

### Monitoring

No specific monitoring required.

### Adverse Effects/Precautions

Occasional reactions include erythema and tenderness at the injection site. Trace components may infrequently cause allergic reactions.

### Pharmacology

Sterile suspension of types 1, 2, and 3 poliovirus inactivated with formaldehyde. The vaccine produced using a microcarrier culture technique of monkey kidney cells has enhanced potency. Contains traces of streptomycin, neomycin, and polymyxin B.

### Special Considerations/Preparation

IPOL® (Sanofi Pasteur) is a clear, colorless suspension, available in 0.5 mL single-dose syringes and multidose vial. Do not use if the vaccine is turbid or discolored. Refrigerate at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

### Selected References

- ◆ American Academy of Pediatrics. Poliovirus Infections. In: Pickering LK, Baker CJ, Kimberlin DW, Long SS, eds. *Red Book: 2009 Report of the Committee on Infectious Diseases*. 28th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009: pp 542-543.
- ◆ Advisory Committee on Immunization Practices: ACIP Recommendations. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/vaccines/pubs/acip-list.htm>
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases: Poliomyelitis prevention: recommendations for use of inactivated poliovirus vaccine and live oral poliovirus vaccine. *Pediatrics* 1997;99:300.
- ◆ Product information, Sanofi Pasteur, 2005

References updated 7/2009





**Dose & Administration**

**Protein C Deficiency, Prevention and Treatment of Venous Thrombosis and Purpura Fulminans:**

**Acute Episode/Short-term Prophylaxis:**

**Initial dose:** 100 to 120 international units/kg IV, followed by 60 to 80 international units/kg IV every 6 hours for next 3 doses.

**Maintenance dose:** 45 to 60 international units/kg IV every 6 or 12 hours.

Dose regimen should be adjusted to maintain a target peak protein C activity of 100%. After resolution of acute episode, maintain trough protein C activity level above 25% for duration of treatment. Continue treatment until desired anticoagulation is achieved.

**Long-term Prophylaxis:** 45 to 60 international units/kg IV every 12 hours. Maintain trough protein C activity level above 25%.

**Administration:** Administer by IV infusion at a maximum rate of 0.2 mL/kg/minute.

**Uses**

Treatment of patients with severe congenital Protein C deficiency for the prevention and treatment of venous thrombosis and purpura fulminans. Also indicated as a replacement therapy.

For patients beginning warfarin therapy (vitamin K antagonist therapy), continue protein C until stable anticoagulation is achieved. Begin warfarin therapy at a low dose and titrate up to desired anticoagulation.

**Monitoring**

Measure plasma level of protein C before and during treatment. During acute thrombotic events, measure protein C activity immediately before the next dose until the patient is stabilized; dose regimen should be adjusted to maintain a target peak protein C activity of 100% (1 international unit/mL). After stabilization, maintain trough protein C activity level above 25% (0.25 international units/mL). Monitor coagulation parameters (including platelet count) during therapy. Closely monitor patients with renal impairment for sodium overload (contains greater than 200 mg of sodium in maximum daily dose).

**Adverse Effects/Precautions**

Patients receiving protein C and initiating oral anticoagulant therapy are at increased risk for warfarin-induced skin necrosis. Most serious and common adverse events reported were hypersensitivity or allergic reactions and lightheadedness. Made from human blood. Bleeding episodes were reported in clinical studies. Product contains small amount of heparin. Patients with renal impairment may experience sodium overload (contains greater than 200 mg of sodium in maximum daily dose).

*continued...*

### Pharmacology

Protein C, a precursor of a vitamin K-dependent anticoagulant glycoprotein, is activated by the thrombin/thrombomodulin-complex on the endothelial cell surface resulting in subsequent potent anticoagulant effects. Once activated, protein C inactivates the activated forms of factors V and VIII with subsequent reduction in thrombin formation. Other effects include profibrinolytic effects. The pharmacokinetic profile in children has not been studied extensively. One pharmacokinetic analysis determined a half-life of 4.2 to 8.3 hours and a recovery of about 44% after infusion in children. Limited data also suggests a faster clearance and larger volume of distribution in young children which may lead to significantly reduced C<sub>max</sub> and therefore, reduced systemic exposure compared to older subjects.

### Special Considerations/Preparation

Available in single-dose vials that contain nominally 500 (blue color bar) or 1000 (green color bar) international units human protein C. Vials should be brought to room temperature and reconstituted with 5 mL and 10 mL of sterile water for injection, respectively, to provide a concentration of 100 international units/mL. Should be used within 3 hours of reconstitution. A filter needle should be used to withdraw dose from vial. When reconstituted, contains the following excipients: human albumin 8 mg/mL, trisodium citrate dihydrate 4.4 mg/mL, and sodium chloride 8.8 mg/mL. **Store unopened vials at 2 to 8 degrees C and protect from light. Avoid freezing.**

### Selected References

- ◆ Knoebf PN: Severe congenital protein C deficiency: The use of protein C concentrates (human) as replacement therapy for life-threatening blood-clotting complications. *Biologics: Targets & Therapy* 2008;2:285-296.
- ◆ Tcheng WY, Dovat S, Gurel Z, et al: Severe congenital protein C deficiency: Description of a new mutation and prophylactic protein C therapy and in vivo pharmacokinetics. *J Pediatr Hematol Oncol* 2008;30:166-171.
- ◆ Dreyfus M, Masterson M, David M, et al: Replacement therapy with a monoclonal antibody purified protein C concentrate in newborns with severe congenital protein C deficiency. *Semin Thromb Hemost* 1995;21:371-381.
- ◆ Product Information, Baxter, 2007.

Added 1/2010

**Dose & Administration**

1 mL per dose.

FOR ORAL USE ONLY. NOT FOR INJECTION.

The Rotarix® vaccine is a 2-dose series with at least 4 weeks between each dose. The recommended vaccination schedule is 2 months of age (minimum age 6 weeks and maximum age 14 weeks 6 days) and 4 months of age (maximum age 8 months). Please refer to the most recent AAP/ACIP immunization recommendations.

To administer the vaccine: 1) Connect transfer adapter onto vial of lyophilized vaccine. 2) Shake the oral applicator containing the liquid diluent (white, turbid suspension). 3) Connect the oral applicator to the transfer adapter. 4) Push plunger of oral applicator to transfer diluent into vial (suspension will appear white and turbid). 5) Withdraw the entire mixture back into the oral applicator. 6) Twist and remove the oral applicator from the transfer adapter. 7) With infant seated in a reclining position, administer orally the entire contents of the oral applicator (on the inside of the cheek). Refer to package insert for illustrations.

If the infant spits out or regurgitates most of the vaccine dose, a single replacement dose is NOT recommended, since this was not studied in clinical trials. There are no restrictions on the infant's liquid consumption (including breast milk) before or after vaccination.

**Uses**

Immunoprophylaxis against rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9).

**Adverse Effects/Precautions**

Vaccination contraindicated in infants with a history of uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant for intussusceptions, in infants with a history of intussusceptions, and in infants with a history of Severe Combined Immunodeficiency Disease (SCID). Infants with severe latex allergy (anaphylaxis) should not receive Rotarix® (oral applicator contains latex rubber). Vaccination should be deferred in infants with acute moderate to severe gastroenteritis, and infants with moderate to severe acute illness.

In a safety and efficacy study (n=63,22 infants), no increased risk of intussusceptions was observed in infants receiving Rotarix® when compared with placebo. There were 6 cases of intussusceptions reported in the Rotarix® infants versus 7 cases in the placebo infants within 31 days after any dose. In a birth cohort from Mexico, interim postmarketing safety data suggested an increased risk of intussusceptions within 31 days of the first dose (relative risk, 1.8; 99% CI, 1 to 3.1), with most cases occurring in the first 7 days post-vaccination.

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Kawasaki disease was reported in 18 (0.035%) recipients of Rotarix® and 9 (0.021%) placebo recipients from 16 completed or ongoing trials. Of the 27 cases, 5 occurred following Rotarix® in clinical trials that were either not placebo-controlled or 1:1 randomized. Three of the 27 cases (2 cases Rotarix® and 1 case placebo) were reported within 30 days post-vaccination. Kawasaki disease was reported in 17 Rotarix® recipients and 9 placebo recipients (relative risk, 1.71; 95% CI, 0.71 to 4.38) in placebo-controlled trials. Among recipients of Rotarix®, the time of onset after study dose ranged from 3 days to 19 months.

### Pharmacology

Rotarix® is a human-derived rotavirus vaccine from the 89-12 strain, which belongs to G1P[8] type. The lyophilized vaccine contains amino acids, dextran, Dulbecco's Modified Eagle Medium, sorbitol, and sucrose. The liquid diluent contains calcium carbonate (to protect the vaccine during passage through the stomach and prevent inactivation), sterile water, and xanthan.

Fecal shedding after vaccination was reported in approximately 26% of vaccinated infants, in two studies. Peak excretion occurred around day 7 after the first dose. Transmission of virus was not evaluated, and the potential for transmission of vaccine virus is not known. Approximately 80% of Rotarix® recipients will be seroconverted one to two months after a 2-dose series.

### Special Considerations/Preparation

Rotarix® is supplied as a vial of lyophilized vaccine, a prefilled oral applicator of liquid diluent (1 mL) with a plunger stopper, and a transfer adapter for reconstitution. The vaccine contains no preservatives. Oral applicator contains latex rubber. Lyophilized vials should be refrigerated and protected from light, and the diluent can be stored at room temperature.

**Do not freeze, and discard vaccine if frozen.**

Reconstituted vaccine may be stored refrigerated or at room temperature, and vaccine should be administered within 24 hours of reconstitution. Discard if not used within 24 hours. **Do not mix with other vaccines or solutions.**

### Selected References

- ◆ Centers for Disease Control and Prevention. Prevention of rotavirus gastroenteritis among infants and children. Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2009;58(RR-2):1-24.
- ◆ Vesikari T, Karvonen A, Prymula R, et al: Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study. *Lancet* 2007;370:1757-1763.
- ◆ Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, et al: Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Engl J Med* 2006;354:11-22.
- ◆ Product Information, GlaxoSmithKline, 2010.

Dosing, Adverse Effects/Precautions, Special Considerations, and References updated 12/2010  
Added 7/2008

**Dose & Administration**

2 mL per dose.

FOR ORAL USE ONLY. NOT FOR INJECTION.

The RotaTeq® vaccine is a 3-dose series with at least 4 weeks between each dose. The recommended vaccination schedule is 2 months of age (minimum age 6 weeks and maximum age 14 weeks 6 days), 4 months of age, and 6 months of age (maximum age 8 months). Please refer to the most recent AAP/ACIP immunization schedule.

To administer the vaccine: 1) Tear open the pouch and remove the dosing tube. 2) Clear the fluid from the dispensing tip by holding tube vertically and tapping cap. 3) Puncture the dispensing tip by screwing cap *clockwise* until it becomes tight, then remove the cap by turning it *counterclockwise*. 4) Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty.

If for any reason an incomplete dose is administered (e.g., infant spits or regurgitates the vaccine), a replacement dose is NOT recommended, since this was not studied in the clinical trials.

**Uses**

Immunoprophylaxis against rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4.

**Adverse Effects/Precautions**

**Contraindicated** in infants with Severe Combined Immunodeficiency Syndrome (SCID); vaccine-acquired rotavirus disease, severe diarrhea and prolonged shedding of vaccine virus have been reported in these patients. Vaccination should be deferred in infants with acute moderate to severe gastroenteritis, and infants with moderate to severe acute illness.

In a safety and efficacy phase III study (n=69,274 infants), there were 6 cases of intussusception reported in the RotaTeq® infants compared with 5 cases in the placebo infants within 42 days after any dose. Approximately 14 million doses of RotaTeq® were distributed in the United States as of March, 2008. According to the US Vaccine Adverse Event Reporting System (VAERS) analyses, as of March 31, 2008, the number of confirmed cases of intussusceptions reported during either the 1 to 21 day period or the 1 to 7 day period after receipt of any dose of RotaTeq® did not exceed the number of cases expected to occur by chance alone. This was verified by the Vaccine Safety Datalink (VSD) which concluded that the number of cases of intussusceptions identified that occurred within a 30-day period after receipt of any dose of RotaTeq® was not more than the number of cases expected to occur with chance alone. The data revealed that if an associated risk is present, the risk for intussusception with the first dose of RotaTeq® within the first week after vaccination is not greater than 1 in 25,000 to 50,000 first doses. Similar findings, that rotavirus vaccine was not associated with a higher risk for intussusceptions compared with historical controls, were reported in a prospective surveillance study based on data from the VSD (a large, federally-funded collaboration that includes 8 managed care organizations).

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According to the US Vaccine Adverse Event Reporting System (VAERS), although clinical trial data reported higher (though not statistically significant) Kawasaki disease rates with RotaTeq®, analyses of postmarketing reports (1990 through 2007) of Kawasaki disease did not show an elevated risk with RotaTeq® or other US-licensed vaccines.

Transmission of vaccine virus strains from vaccinees to non-vaccinated contacts has been reported. In clinical studies, vaccine virus shedding was noted from 1 day to 15 days after a dose. Caution is advised when administering vaccine to patients with close contact to individuals with immunodeficiencies (malignancies, primary immunodeficiency, immunocompromised, or receiving immunosuppressive therapy).

### Pharmacology

RotaTeq® is a bovine-based pentavalent vaccine containing 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express 1 of the outer capsid proteins (G1, G2, G3, or G4) from the human rotavirus parent strain and the attachment protein (P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein (P1A[8]) from the human rotavirus parent strain and the outer capsid protein G6 from the bovine rotavirus parent strain. The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell-culture media, and trace amounts of fetal bovine serum. There are no preservatives or thimerosal.

Fecal shedding of vaccine virus occurred in 32 (8.9%) of 360 subjects after dose 1, 0 (0%) of 249 subjects after dose 2, and 1 (0.3%) of 385 subjects after dose 3. In phase III studies, shedding was observed as early as 1 day and as late as 15 days after a dose. The potential for transmission of vaccine virus was not assessed through epidemiologic studies.

RotaTeq® can be coadministered with other childhood vaccines. It has 98% efficacy for prevention of severe illness and 74% for prevention of rotavirus-induced diarrheal episodes.

### Special Considerations/Preparation

RotaTeq® is supplied as a suspension for oral use in individually pouched single-dose tubes. Each dosage tube contains 2 mL. It is a pale yellow clear liquid that may have a pink tint. Store and transport refrigerated. Protect from light. Administer as soon as possible after being removed from refrigeration. Discard in approved biological waste containers.

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**Selected References**

- ◆ Belongia EA, Irving SA, Shui IM, et al: Real-time surveillance to assess risk of intussusception and other adverse events after pentavalent, bovine-derived rotavirus vaccine. *Pediatr Infect Dis* 2010;29:1-5.
- ◆ Patel NC, Hertel PM, Estes MK, et al: Vaccine-acquired rotavirus in infants with severe combined immunodeficiency. *N Engl J Med* 2010;362:314-319.
- ◆ Hua W, Izurieta HS, Slade B, et al: Kawasaki Disease After Vaccination. Reports to the Vaccine Adverse Event Reporting System 1990-2007. *Pediatr Infect Dis J* 2009;28(11):943-947.
- ◆ Centers for Disease Control and Prevention. Prevention of rotavirus gastroenteritis among infants and children. Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2009;58(RR-2):1-24.
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases. Prevention of rotavirus disease: guidelines for use of rotavirus vaccine. *Pediatrics* 2007;119:171-181.
- ◆ Centers for Disease Control and Prevention. Postmarketing monitoring of intussusception after RotaTeg® vaccination - United States, February 1, 2006-February 15, 2007. *MMWR* 2007; 56(10):218-222.
- ◆ Parashar UD, Alexander JP, Glass RI; Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2006;55(RR-12):1-13.
- ◆ Vesikari T, Matson DO, Dennehy P, et al: Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine. *N Engl J Med* 2006;354:23-33.
- ◆ Product information, Merck & Co., 2010.

Adverse Effects/Precautions and References updated 12/2010

Added 3/2007

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## CARDIOVASCULAR DRUGS

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### Dose & Administration

**Starting dose:** 50 mcg/kg rapid IV push (1 to 2 seconds). Increase dose in 50 mcg/kg increments every 2 minutes until return of sinus rhythm. Usual maximum dose: 250 mcg/kg. Infuse as close to IV site as possible. Flush IV with saline immediately. Intraosseous administration has also been reported to be successful.

### Uses

Acute treatment of sustained paroxysmal supraventricular tachycardia. It may also be useful in establishing the cause of the SVT.

### Monitoring

Continuous EKG and blood pressure monitoring.

### Adverse Effects/Precautions

Flushing, dyspnea, and irritability occur frequently, but usually resolve within 1 minute. Transient (duration less than 1 minute) arrhythmias may occur between termination of SVT and onset of normal sinus rhythm. Apnea has been reported in one preterm infant. Recurrence of SVT occurs in approximately 30% of treated patients. Aminophylline/Theophylline and caffeine diminish adenosine's effect by competitive antagonism.

### Pharmacology

Adenosine is the pharmacologically active metabolite of ATP. It acts by depressing sinus node automaticity and A-V node conduction. It does **not** have negative inotropic effects. Response should occur within 2 minutes of the dose. Estimated serum half-life is 10 seconds.

### Special Considerations/Preparation

Supplied in 2 mL vials containing 6 mg adenosine dissolved in NS. Contains no preservative. Store at room temperature. **Do not refrigerate;** crystallization will occur. Solution must be clear at the time of use.

Dilutions can be made with NS for doses less than 0.2 mL (600 mcg). Use 1 mL (3000 mcg) with 9 mL NS to make a solution with a final concentration of 300 mcg/mL.

**Solution Compatibility:** D<sub>5</sub>W and NS.

### Selected References

- ◆ Paret G, Steinmetz D, Kuint J et al: Adenosine for the treatment of paroxysmal supraventricular tachycardia in fullterm and preterm newborn infants. *Am J Perinatol* 1996;13:343-46.
- ◆ Friedman FD: Intraosseous adenosine for the termination of supraventricular tachycardia in an infant. *Ann Emerg Med* 1996;28:356-58.
- ◆ Crosson JE, Etheridge SP, Milstein S et al: Therapeutic and diagnostic utility of adenosine during tachycardia evaluation in children. *Am J Cardiol* 1994;74:155-60.
- ◆ Till J, Shinebourne EA, Rigby ML, et al: Efficacy and safety of adenosine in the treatment of supraventricular tachycardia in infants and children. *Br Heart J* 1989;62:204.
- ◆ Overholt ED, Rhuban KS, Gutgesell HP, et al: Usefulness of adenosine for arrhythmias in infants and children. *Am J Cardiol* 1988;61:336.
- ◆ Product Information, Astellas, 2005

Compatibilities updated 3/2005

Updated 3/1998



**Dose & Administration**

**Initial dose:** 0.05 to 0.1 mcg/kg per minute by continuous IV infusion. Titrate to infant's response—oxygenation *versus* adverse effects.

**Maintenance dose:** May be as low as 0.01 mcg/kg per minute.

Higher initial doses are usually no more effective and have a high incidence of adverse effects.

May also be given via UAC positioned near ductus arteriosus.

**Sample Dilution and Infusion Rate:** Mix 1 ampule (500 mcg) in 49 mL of compatible solution (e.g., D5W) yielding a concentration of 10 mcg/mL. Infuse at a rate of 0.6 mL/kg per hour to provide a dose of 0.1 mcg/kg per minute.

**Uses**

To promote dilation of ductus arteriosus in infants with congenital heart disease dependent on ductal shunting for oxygenation/perfusion.

**Monitoring**

Closely monitor respiratory and cardiovascular status. Assess for improvement in oxygenation. Closely monitor infant's temperature. Ensure reliable IV access: duration of effect is short.

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, apnea has been reported in 10% to 12% of neonates with congenital heart defects treated with alprostadil. Apnea is seen most often in neonates weighing less than 2 kg at birth, and usually appears during the first hour of drug infusion.

**Be prepared to intubate/resuscitate.**

**Common (6% to 15%):** Apnea (consider treating with aminophylline), hypotension, fever, leukocytosis, cutaneous flushing, and bradycardia. Hypokalemia reported with long-term therapy (greater than 20 days), especially with doses greater than 0.05 mcg/kg/minute. Gastric outlet obstruction and reversible cortical proliferation of the long bones after prolonged treatment (greater than 120 hours).

**Uncommon (1% to 5%):** Seizures, hypoventilation, tachycardia, cardiac arrest, edema, sepsis, diarrhea, and disseminated intravascular coagulation.

**Rare (less than 1%):** Urticaria, bronchospasm, hemorrhage, hypoglycemia, and hypocalcemia.

**Musculoskeletal changes:** Widened fontanel, pretibial and soft tissue swelling, and swelling of the extremities may occur after 9 days of therapy. Cortical hyperostosis and periostitis may occur with long-term (greater than 3 months) therapy. These changes resolve over weeks after discontinuation of therapy.

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**Pharmacology**

Alprostadil causes vasodilation of **all** arterioles. Inhibition of platelet aggregation. Stimulation of uterine and intestinal smooth muscle. Maximal drug effect usually seen within 30 minutes in cyanotic lesion; may take several hours in acyanotic lesions.

**Special Considerations/Preparation**

Supplied in 1 mL (500 mcg) ampules that must be refrigerated. **Dilute before administration to a concentration of 20 mcg/mL or less.** Prepare fresh infusion solutions every 24 hours. Osmolality of undiluted (500 mcg/mL) is 23,250 mOsm/kg. Extravasation may cause tissue sloughing and necrosis.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Dex/AA Solutions. Aminophylline, ampicillin, caffeine citrate, calcium chloride, cefazolin, cefotaxime, chlorothiazide, cimetidine, clindamycin, dobutamine, dopamine, fentanyl, furosemide, gentamicin, glycopyrrolate, metoclopramide, metronidazole, nitroglycerin, nitroprusside, potassium chloride, penicillin G, tobramycin, vancomycin, and vecuronium.

**Selected References**

- ♦ Meckler GD, Lowe C: To intubate or not to intubate? Transporting infants on prostaglandin E<sub>1</sub>. *Pediatrics* 2009;123:e25-e30.
- ♦ Talosi G, Katona M, Turi S: Side-effects of long-term prostaglandin E<sub>1</sub> treatment in neonates. *Pediatr Int* 2007;49:335-340.
- ♦ Dice JE: Physical compatibility of alprostadil with commonly used IV solutions and medications in the neonatal intensive care unit. *J Pediatr Pharmacol Ther* 2006;11:233-236.
- ♦ Lim DS, Kulik TJ, Kim DW: Aminophylline for the prevention of apnea during prostaglandin E<sub>1</sub> infusion. *Pediatrics* 2003;112:e27-e29.
- ♦ Arav-Boger R, Baggett HC, Spevak PJ, Willoughby RE: Leukocytosis caused by prostaglandin E<sub>1</sub> in neonates. *J Pediatr* 2001;138:263-265.
- ♦ Kaufman MB, El-Chaar GM: Bone and tissue changes following prostaglandin therapy in neonates. *Ann Pharmacother* 1996;30:269.
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- ♦ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 250.
- ♦ Lewis AB, Freed MD, Heymann MA, et al: Side effects of therapy with prostaglandin E<sub>1</sub> in infants with congenital heart disease. *Circulation* 1981;64:893.
- ♦ Heymann MA: Pharmacologic use of prostaglandin E<sub>1</sub> in infants with congenital heart disease. *Am Heart J* 1981;101:837.
- ♦ Product Information, Pfizer, 2002

Compatibilities updated 8/2010

Adverse effects and References updated 1/2009

**Dose & Administration**

**Restoration of function to central venous catheter:** Instill into dysfunctional catheter at a concentration of 1 mg/mL. Use 110% of the internal lumen volume of the catheter, not to exceed 2 mg in 2 mL. If catheter function is not restored in 120 minutes after 1 dose, a second dose may be instilled.

**Dissolution of intravascular thrombi:** 200 mcg/kg per hour (0.2 mg/kg per hour). Duration of therapy is 6 to 48 hours. If administering directly into the thrombus, dose may be increased after 6 hours to a maximum of 500 mcg/kg per hour. If localized bleeding occurs, stop infusion for 1 hour and restart using 100 mcg/kg per hour. Discontinue heparin several hours prior to initiation of therapy.

**Note:** Reports in the literature are a collection of cases gathered over several years. Some authors used loading doses, others did not. Infused doses ranged from 20 to 500 mcg/kg per hour. Complications were most often linked with higher doses and longer duration of therapy. Call 1-800-NOCLOTS for case reporting and treatment guidance.

**Uses**

Dissolution of intravascular thrombi of recent onset that are either intraarterial or life-threatening. Adjuvant treatment of infective endocarditis vegetations.

**Monitoring**

Follow coagulation studies (PT, aPTT, fibrinogen, fibrin split products) prior to therapy and at least daily during treatment. Maintain fibrinogen levels greater than 100 mg/dL and platelets greater than 50,000/mm<sup>3</sup>. Echocardiography to assess clot lysis at least every 12 hours (every 6 hours optimal). Cranial ultrasound to assess for hemorrhage prior to therapy.

**Adverse Effects/Precautions**

Intracranial hemorrhage may occur, especially in premature infants treated for prolonged periods. Bleeding from venipuncture sites occurs in approximately half of treated patients. The risk of complications increases at doses above 450 mcg/kg per hour.

**Pharmacology**

Alteplase binds strongly and specifically to fibrin in a thrombus and converts the entrapped plasminogen to plasmin. This initiates local fibrinolysis with limited systemic proteolysis. Alteplase has a shorter half-life than streptokinase and does not cause anaphylactic reactions. It is cleared rapidly from the plasma, primarily via the liver.

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**Special Considerations/Preparation**

Activase® is supplied as lyophilized powder in 50 mg and 100 mg vials. Reconstitute 50 mg vial by adding 50 mL sterile water for injection (do not use bacteriostatic water for injection) for a concentration of 1 mg/mL. Can be further diluted with NS or D<sub>5</sub>W to a concentration of 0.5 mg/mL if necessary. Use reconstituted solution within 8 hours of mixing when stored refrigerated or at room temperature.

Cathflo® Activase® is supplied as lyophilized powder in 2 mg vials. Reconstitute by adding 2.2 mL sterile water for injection to a final concentration of 1 mg/mL. Do not use bacteriostatic water for injection. Mix by gently swirling until the contents are completely dissolved. DO NOT SHAKE. Use reconstituted solution within 8 hours of mixing. Reconstituted solution may be stored refrigerated or at room temperature.

**Solution Compatibility:** NS and D<sub>5</sub>W.

**Terminal Injection Site Compatibility:** Lidocaine, morphine, nitroglycerin, and propranolol.

**Incompatibility:** Dobutamine, dopamine, and heparin.

**Selected References**

- ♦ Manco-Johnson M, Nuss R: Neonatal thrombotic disorders. *NeoReviews* 2000;1:e201.
- ♦ Hartmann J, Hussein A, Trowitzsch E, et al: Treatment of neonatal thrombus formation with recombinant tissue plasminogen activator: six years experience and review of the literature. *Arch Dis Child Fetal Neonatal Ed* 2001;85:F18-F22.
- ♦ Marks KA, Zucker N, Kapelushnik J, et al: Infective endocarditis successfully treated in extremely low birth weight infants with recombinant tissue plasminogen activator. *Pediatrics* 2002;109:153-158.
- ♦ Weiner GM, Castle VP, DiPietro MA, Faix RG: Successful treatment of neonatal arterial thromboses with recombinant tissue plasminogen activator. *J Pediatr* 1998;133:133-136.
- ♦ Product Information, Genentech, Inc., 2005.

Preparation updated 3/2008

Dose & Administration and Compatibilities updated 3/2005

**Dose & Administration**

**IV Loading dose:** 5 mg/kg IV infusion given over 30 to 60 minutes, preferably in a central vein.

**Maintenance infusion:** 7 to 15 mcg/kg per minute (10 to 20 mg/kg per 24 hours). Begin at 7 mcg/kg per minute and titrate by monitoring effects. For infusions lasting longer than 1 hour, amiodarone IV concentrations should not exceed 2 mg/mL unless using a central line.

**Consider switching to oral therapy within 24 to 48 hours.**

**Oral:** 5 to 10 mg/kg per dose every 12 hours.

**Uses**

Treatment of life-threatening or drug-resistant refractory supraventricular (SVT), ventricular tachyarrhythmias (VT), and postoperative junctional ectopic tachycardia (JET) - see Adverse Effects.

**Monitoring**

Continuous EKG and blood pressure (for IV). Follow AST and ALT. Monitor T<sub>3</sub>, T<sub>4</sub>, and TSH. Observe IV site for extravasation.

**Adverse Effects/Precautions**

**Short term toxicity:** Bradycardia and hypotension (possibly associated with rapid rates of infusion). In a study of pediatric patients (n=61), ages 30 days to 15 years, hypotension and bradycardia were reported in 36% and 20% of patients, respectively. AV block was reported in 15% of patients. Polymorphic ventricular tachycardia may occur. Irritating to the peripheral vessels (concentrations greater than 2 mg/mL). Administration through central vein preferred.

**Long term toxicity:** Hyperthyroidism (due to inhibition of T<sub>4</sub> to T<sub>3</sub>) and hypothyroidism (due to high concentration of inorganic iodine). Generic formulation contains 2% benzyl alcohol (20 mg/mL). Hepatitis and cholestatic hepatitis (rare). Photosensitivity (10%), nausea and vomiting (10%), optic neuritis (4% to 9%), and pulmonary fibrosis (4% to 9%) have been reported with prolonged oral use in adults.

**Black Box Warning**

According to the manufacturer's black box warning, a potentially fatal toxicity associated with amiodarone is hypersensitivity pneumonitis or interstitial/alveolar pneumonitis (reported in adults). Liver injury is common but usually mild. Amiodarone may exacerbate an existing arrhythmia.

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**Pharmacology**

Class III antiarrhythmic agent that is an iodinated benzofuran compound. Electrophysiologic activity is accomplished by prolonging the duration of the action potential and increasing the effective refractory period. Increases cardiac blood flow and decreases cardiac work and myocardial oxygen consumption. Highly protein bound (95%) in adults. Extensively metabolized to an active metabolite by the cytochrome CYP3A4 isoenzyme system (limited in preterm infants). Drug-drug interaction potentially occur when given in combination with drugs that inhibit cytochrome CYP3A4: phenytoin, fosphenytoin, clarithromycin, erythromycin, azole antifungals (e.g. fluconazole, ketoconazole, itraconazole), protease inhibitors (e.g. indinavir, ritonavir), class IA and class III antiarrhythmics (e.g. quinidine, procainamide, sotalol) and cimetidine (amiodarone levels increase). Amiodarone prevents the elimination of digoxin resulting in high digoxin levels. Half-life reported to be 26 to 107 days in adults. No data in preterm infants. Accumulates in tissues; serum levels can be detected for months. Contains 37.3% iodine by weight. Adheres to PVC tubing: low infusion rates in neonates may lead to reduced drug delivery during continuous infusions. Oral absorption is variable with approximately 50% bioavailability.

**Special Considerations/Preparation**

**IV:** The preferred formulation is Nexterone®, available as 1.5 mg/mL (150 mg/100 mL) and 1.8 mg/mL (360 mg/200 mL) concentrations in premix bags. Nexterone® does not contain benzyl alcohol or polysorbate 80, and therefore does not carry a warning regarding benzyl alcohol and fatal gasping syndrome in neonates. There are also no limitations regarding compatibility and stability with plastics and isotonic infusion fluids. Store at room temperature and protect from light.

Generic amiodarone is also available as 50 mg/mL concentration in 5, 10, and 20 mL vials. Contains 2% (20 mg/mL) of benzyl alcohol and 10% (100 mg/mL) polysorbate (Tween) 80 as a preservative. Store at room temperature and protect from light.

**Oral:** Supplied in 200 mg tablets. An oral suspension with a final concentration of 5 mg/mL may be made as follows: crush a 200 mg tablet, slowly mix in 20 mL of 1% methylcellulose, then add in 20 mL of simple syrup to make a total volume of 40 mL. Stable for six weeks at room temperature and three months refrigerated when stored in glass or plastic.

**Solution Compatibility:** D<sub>5</sub>W, and NS at concentrations of 1 to 6 mg/mL.

**Solution Incompatibility:** No data available for Dex/AA solutions.

*continued...*



**Terminal Injection Site Compatibility:** (Data for old formulation): Amikacin, amphotericin B, atropine, calcium chloride, calcium gluconate, ceftizoxime, ceftriaxone, cefuroxime, clindamycin, dobutamine, dopamine, epinephrine, famotidine, fentanyl, fluconazole, furosemide, esmolol, erythromycin, gentamicin, insulin, isoproterenol, lidocaine, lorazepam, metronidazole, midazolam, milrinone, morphine, nitroglycerin, norepinephrine, penicillin G, phenolamine, potassium chloride, procainamide, tobramycin, vancomycin, and vecuronium.

**Incompatibility:** (Data for old formulation): Aminophylline, ampicillin, ceftazidime, cefazolin, digoxin, heparin, imipenem-cilastatin, mezlocillin, micafungin, piperacillin, piperacillin-tazobactam, sodium bicarbonate, and sodium nitroprusside. No data available for Dex/AA solutions.

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Compatibilities updated 7/2009

Adverse Effects/Precautions, Special Considerations, and References updated 1/2009

Added 3/2001



**Dose & Administration**

**IV:** 0.01 to 0.03 mg/kg per dose IV over 1 minute, or IM.

Dose can be repeated every 10 to 15 minutes to achieve desired effect, with a maximum total dose of 0.04 mg/kg.

**ET:** 0.01 to 0.03 mg/kg per dose immediately followed by 1 mL NS.

**Oral:** Begin with 0.02 mg/kg per dose given every 4 to 6 hours. May increase gradually to 0.09 mg/kg per dose.

**Uses**

Reversal of severe sinus bradycardia, particularly when parasympathetic influences on the heart (digoxin, beta-blocker drugs, hyperactive carotid sinus reflex) predominate. Also used to reduce the muscarinic effects of neostigmine when reversing neuromuscular blockade.

**Monitoring**

Heart rate.

**Adverse Effects/Precautions**

Cardiac arrhythmias can occur, particularly during the first 2 minutes following IV administration; usually a simple A-V dissociation, more often caused by smaller rather than larger doses. Fever, especially in brain-damaged infants. Abdominal distention with decreased bowel activity. Esophageal reflux. Mydriasis and cycloplegia.

**Pharmacology**

Anticholinergic. Increases heart rate by decreasing the effects of the parasympathetic system while increasing the effects of the sympathetic system. Peak tachycardia is 12 to 16 minutes after dose is given. Relaxes bronchial smooth muscle, thus reducing airway resistance and increasing dead space by 30%. Motor activity in the stomach and small and large intestines is reduced. Esophageal sphincter tone is reduced. Salivary secretion is inhibited. Duration of action is 6 hours. Primarily excreted renally unchanged.

**Special Considerations/Preparation**

Supplied in multiple concentrations (0.05-, 0.1-, 0.4-, and 1-mg/mL) for injection. Give IV dosage form orally. Prepare IV or oral dilution by mixing 1 mL of injectable atropine (0.4 mg/mL) in 7 mL of sterile water for injection to yield final concentration of 0.05 mg/mL. Stable for 28 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Amiodarone, cimetidine, dobutamine, famotidine, fentanyl, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, meropenem, methadone, metoclopramide, midazolam, milrinone, morphine, nafcillin, netilmicin, pentobarbital, potassium chloride, propofol, ranitidine, and sodium bicarbonate.

**Incompatibility:** Phenytoin, sulfamethoxazole/trimethoprim.

*continued...*

**Selected References**

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- ◆ Product Information, Hospira, 2004.

Compatibilities updated 7/2009

**Dose & Administration**

**Initial dose:** 0.01 to 0.05 mg/kg per dose orally every 8 to 12 hours. Adjust dose and interval based on response. Administer 1 hour before feeding.

**Uses**

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

**Monitoring**

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

**Adverse Effects/Precautions**

Neonates are more sensitive to the effects of captopril than are older infants and children. Significant decreases in cerebral and renal blood flow have occurred in premature infants with chronic hypertension who received higher doses (0.15 to 0.30 mg/kg per dose) than those recommended above. These episodes occurred unpredictably during chronic therapy, and some were associated with neurologic (seizures, apnea, lethargy) and renal (oliguria) complications. **The use of captopril is contraindicated in patients with bilateral renovascular disease or with unilateral renal artery stenosis in a solitary kidney, as the loss of adequate renal perfusion could precipitate acute renal failure.** Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements.

**Pharmacology**

Captopril is an angiotensin-converting enzyme (ACE) inhibitor that blocks the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Captopril also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Bioavailability is good in neonates, although food will decrease absorption. Onset of action is 15 minutes after a dose, with peak effects seen in 30 to 90 minutes. Duration of action is usually 2 to 6 hours, but may be significantly longer (greater than 24 hours).

**Special Considerations/Preparation**

Available in 12.5-mg, 25-mg, 50-mg, and 100-mg tablets.

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**Oral Suspension** Aqueous captopril solutions have been reported to degrade rapidly, and stability in different solutions is highly variable and dependent on many factors (pH, type of vehicle, drug concentration, addition of preservative). There have been conflicting results in various studies over the years. The data below represents some of the studies of various extemporaneously prepared captopril oral solutions.

Captopril 1 mg/mL oral solution made with tablets and undiluted syrup was stable for 30 days refrigerated (5 degrees C). In this study, different formulations of captopril solutions were made using either tablets or powder with different vehicles used (sterile water, syrup, methylcellulose); edetate disodium was added to some of the formulations. Better stability was noted when captopril tablets were used compared with powder, with undiluted versus diluted syrup as the vehicle, and when edetate disodium was added as the preservative.

Captopril oral suspension can be made by dissolving 6.25 mg (one-half of a scored 12.5-mg tablet) in 10 mL of sterile water, adding 1000 mg of sodium ascorbate for injection (4 mL of 250-mg/mL solution) to decrease oxidation, then adding sufficient water to make a final volume of 200 mL. The final concentration is 0.03 mg/mL captopril and 5 mg/mL sodium ascorbate. Solution is stable for 14 days at room temperature, 56 days refrigerated. Some undissolved excipients will remain visible.

To overcome potential stability problems, powder papers and compounded capsules have been utilized to extemporaneously prepare captopril solutions just prior to administration.

### Selected References

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Special Considerations and References updated 12/2010.  
Added 1/1994.

**Dose & Administration**

**Loading doses:** ("Digitalization") are generally used only when treating arrhythmias and acute congestive heart failure. Give over 24 hours as 3 divided doses. Administer IV slow push over 5 to 10 minutes.

Oral doses should be 25% greater than IV doses. Do not administer IM.

**Note:** These beginning doses are based primarily on studies that measured echocardiographic changes and EKG signs of toxicity and take into account renal maturation. We recommend titrating dosage based on clinical response. Decrease dose proportional to the reduction in creatinine clearance.

**Total Loading Dose**

PMA weeks	IV mcg/kg	PO mcg/kg
≤29	15	20
30 to 36	20	25
37 to 48	30	40
≥49	40	50
Divide into 3 doses over 24 hours.		

**Maintenance Doses**

PMA weeks	IV mcg/kg	PO mcg/kg	Interval hours
≤29	4	5	24
30 to 36	5	6	24
37 to 48	4	5	12
≥49	5	6	12
Titrate based on clinical response.			

**Uses**

Treatment of heart failure caused by diminished myocardial contractility. Treatment of SVT, atrial flutter, and atrial fibrillation.

**Monitoring**

Follow heart rate and rhythm closely. Periodic EKGs to assess both desired effects and signs of toxicity. Follow closely (especially in patients receiving diuretics or amphotericin B) for decreased serum potassium and magnesium, or increased calcium and magnesium, all of which predispose to digoxin toxicity. Assess renal function. Be aware of drug interactions. May follow serum drug concentrations if assay is available that excludes endogenous digoxin-like substances. Therapeutic serum concentration is 1 to 2 ng/mL.

**Adverse Effects/Precautions****Toxic Cardiac Effects:**

- PR interval prolongation
- Sinus bradycardia or SA block
- Atrial or nodal ectopic beats
- Ventricular arrhythmias

**Nontoxic Cardiac Effects:**

- QTc interval shortening
- ST segment sagging
- T-wave amplitude dampening
- Heart rate slowing

**Other Effects:** Feeding intolerance, vomiting, diarrhea, and lethargy.

**Treatment of Life-Threatening Digoxin Toxicity:**

**Digibind®** Digoxin Immune Fab, IV over 30 minutes through 0.22 micron filter.

$$\text{Dose (\# of vials)} = \frac{(\text{weight [kg]}) \times (\text{serum digoxin concentration})}{100}$$

Each vial of Digibind® contains 38 mg (enough to bind 0.5 mg digoxin).

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### Pharmacology

Digitalis glycoside with positive inotropic and negative chronotropic actions. Increases myocardial catecholamine levels (low doses) and inhibits sarcolemmal sodium-potassium-ATPase (higher doses) to enhance contractility by increasing systolic intracellular calcium-ion concentrations. Indirectly increases vagal activity, thereby slowing S-A node firing and A-V node conduction. Other effects include peripheral, splanchnic, and perhaps, pulmonary vasoconstriction, and reduced CSF production. Serum concentration peaks 30 to 90 minutes after an oral dose, with myocardial peak occurring in 4 to 6 hours. Large volume of distribution that increases with age during infancy. Rapid absorption of oral dose from small intestine; reduced by antacids and rapid transit times. 20% protein bound. Probably not significantly metabolized. Glomerular filtration and tubular secretion account for most of the total body clearance of digoxin, although significant nonrenal elimination has been proposed.

### Special Considerations/Preparation

**Pediatric dosage forms:** Injectable (100 mcg/mL) and elixir (50 mcg/mL).

Store at room temperature and protect from light. Dilute injectable as follows:

- 1) Draw up digoxin into syringe.
- 2) Inject desired amount of drug into second syringe containing a fourfold or greater volume of solution-compatible diluent. Use diluted product immediately.

**Drug Interactions:** Amiodarone, indomethacin, spironolactone, quinidine, and verapamil decrease digoxin clearance. Cisapride and metoclopramide decrease digoxin absorption. Spironolactone interferes with radioimmunoassay. Erythromycin may increase digoxin absorption.

**Solution Compatibility: (only when diluted fourfold or greater):** D<sub>5</sub>W, D<sub>10</sub>W, NS, and sterile water for injection.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Cimetidine, famotidine, furosemide, heparin, hydrocortisone succinate, insulin, lidocaine, linezolid, meropenem, midazolam, milrinone, morphine, potassium chloride, ranitidine, and remifentanyl.

**Incompatibility:** Amiodarone, dobutamine, fluconazole, and propofol.

### Selected References

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Compatibilities updated 7/2009

References updated 3/2004

Special Considerations updated 3/2002



**Dose & Administration**

2 to 25 mcg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV.

**Solution Preparation Calculations**

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

**Example (for Dobutamine):** Mix 30 mL of 800 mcg/mL solution using dobutamine concentration of 12.5 mg/mL.

800 mcg/mL = 0.8 mg/mL

0.8 mg/mL x 30 mL = 24 mg dobutamine

$$\frac{\text{*24 mg}}{\text{12.5 mg/mL}} = 1.9 \text{ mL of dobutamine}$$

Add 1.9 mL of dobutamine (12.5 mg/mL) to 28.1 mL of compatible solution (eg, D<sub>5</sub> W) to yield 30 mL of infusion solution with a concentration of 800 mcg/mL.

**Dobutamine Titration Chart**

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
500	2.5	0.3
	5	0.6
	7.5	0.9
	10	1.2
800	2.5	0.19
	5	0.38
	7.5	0.56
	10	0.75
1000	2.5	0.15
	5	0.3
	7.5	0.45
	10	0.6
1600	2.5	0.094
	5	0.19
	7.5	0.28
	10	0.38
2000	2.5	0.075
	5	0.15
	7.5	0.23
	10	0.3
3200	2.5	0.047
	5	0.094
	7.5	0.14
	10	0.19
4000	2.5	0.038
	5	0.075
	7.5	0.11
	10	0.15

*continued...*

**Uses**

Treatment of hypoperfusion and hypotension, especially if related to myocardial dysfunction.

**Monitoring**

Continuous heart rate and intra-arterial blood pressure monitoring preferable. Observe IV site for signs of extravasation.

**Adverse Effects/Precautions**

May cause hypotension if patient is hypovolemic. Volume loading is recommended before starting dobutamine therapy. Tachycardia occurs at high dosage. Arrhythmias, hypertension, and cutaneous vasodilation. Increases myocardial oxygen consumption. Tissue ischemia occurs with infiltration.

**Pharmacology**

Synthetic catecholamine with primarily  $\beta_1$ -adrenergic activity. Inotropic vasopressor. Increases myocardial contractility, cardiac index, oxygen delivery, and oxygen consumption. Decreases systemic and pulmonary vascular resistance (adults). Dobutamine has a more prominent effect on cardiac output than dopamine but less of an effect on blood pressure. Onset of action is 1 to 2 minutes after IV administration, with peak effect in 10 minutes. Must be administered by continuous IV infusion because of rapid metabolism of drug. Serum half-life is several minutes. Metabolized in the liver by sulfoconjugation to an inactive compound. There is wide interpatient variability in plasma clearance due to differences in metabolism and renal excretion.

**Special Considerations/Preparation**

Supplied as 250 mg per 20-mL vial (12.5 mg/mL) and premixed bags in concentrations of 1, 2, and 4 mg/mL. Diluted solutions for infusion should be used within 24 hours. Solutions containing dobutamine and dextrose may exhibit a pink color which will increase with time due to oxidation of the drug. There is no significant loss of potency.

There are no specific data regarding the compatibility of dobutamine and fat emulsions. Dobutamine is most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dobutamine and fat emulsion together; dobutamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>5</sub>NS, D<sub>10</sub>W, LR, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Alprostadil, amiodarone, atropine, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, caspofungin, ceftazidime, ciprofloxacin, dopamine, enalaprilat, epinephrine, famotidine, fentanyl, fluconazole, flumazenil, heparin, hydralazine, insulin, isoproterenol, lidocaine, linezolid, lorazepam, magnesium sulfate, meropenem, midazolam, milrinone, morphine, nifedipine, nitroglycerin, nitroprusside, pancuronium bromide, phentolamine, potassium chloride, procainamide, propofol, propranolol, ranitidine, remifentanyl, vecuronium, and zidovudine.

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**Incompatibility:** Acyclovir, alteplase, aminophylline, cefepime, bumetanide, diazepam, digoxin, furosemide, ibuprofen lysine, indomethacin, micafungin, phenytoin, phytonadione, piperacillin-tazobactam, and sodium bicarbonate.

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- ◆ Product Information, Hospira, 2005.

Special Considerations and References updated 12/2010

Incompatibility updated 10/2009

Compatibilities updated 7/2009



**Dose & Administration**

2 to 20 mcg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV.

**Solution Preparation Calculations**

To calculate the **AMOUNT** of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the **VOLUME** of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

**Example (for Dopamine):** Mix 30 mL of 800 mcg/mL solution using dopamine concentration of 40 mg/mL.

800 mcg/mL = 0.8 mg/mL

0.8 mg/mL x 30 mL = 24 mg dopamine

$$\frac{24 \text{ mg}}{40 \text{ mg/mL}} = 0.6 \text{ mL of dopamine}$$

Add 0.6 mL of dopamine (40 mg/mL) to 29.4 mL of compatible solution (eg, D<sub>5</sub> W) to yield 30 mL of infusion solution with a concentration of 800 mcg/mL.

**Dopamine Titration Chart**

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
500	2.5	0.3
	5	0.6
	7.5	0.9
	10	1.2
800	2.5	0.19
	5	0.38
	7.5	0.56
	10	0.75
1000	2.5	0.15
	5	0.3
	7.5	0.45
	10	0.6
1600	2.5	0.094
	5	0.19
	7.5	0.28
	10	0.38
2000	2.5	0.075
	5	0.15
	7.5	0.23
	10	0.3
3200	2.5	0.047
	5	0.094
	7.5	0.14
	10	0.19

*continued...*

**Uses**

Treatment of hypotension.

**Monitoring**

Continuous heart rate and intra-arterial blood pressure monitoring is preferable. Assess urine output and peripheral perfusion frequently. Observe IV site closely for blanching and infiltration.

**Adverse Effects/Precautions**

Tachycardia and arrhythmias. May increase pulmonary artery pressure. Reversible suppression of prolactin and thyrotropin secretion.

**Black Box Warning**

Tissue sloughing may occur with IV infiltration. According to the manufacturer's black box warning, to prevent sloughing and necrosis in areas of extravasation, the area should be infiltrated as soon as possible with a saline solution containing phentolamine mesylate.

**Suggested treatment:** Inject a 0.5 mg/mL solution of phentolamine into the affected area. The usual amount needed is 1 to 5 mL, depending on the size of the infiltrate.

**Pharmacology**

Catecholamine. Metabolized rapidly. Serum half-life is 2 to 5 minutes, but clearance is quite variable.

Dopamine increases blood pressure primarily by increasing systemic vascular resistance via  $\alpha$ -adrenergic effects. Effects on cardiac output vary with gestational age and baseline stroke volume. Selective renal vasodilation associated with increases in urine output has been noted in preterm neonates at doses of 2 to 5 mcg/kg/minute. No changes in mesenteric or cerebral blood flow were observed. Mechanism of action in neonates is controversial. Relative effects of dopamine at different doses are uncertain because of developmental differences in 1) endogenous norepinephrine stores, 2)  $\alpha$ -adrenergic,  $\beta$ -adrenergic, and dopaminergic receptor functions, and 3) the ability of the neonatal heart to increase stroke volume. Responses tend to be individualized. Use higher doses with caution in patients with persistent pulmonary hypertension of the newborn.

**Special Considerations/Preparation**

Available in 40-mg/mL, 80-mg/mL, and 160-mg/mL vials for injection and premixed bags in concentrations of 800-, 1600-, and 3200-mcg/mL. Diluted solutions stable for 24 hours. **Admixtures exhibiting a color change should not be used.**

There are no specific data regarding the compatibility of dopamine and fat emulsions. Dopamine is most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dopamine and fat emulsion together; dopamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>5</sub>NS, D<sub>10</sub>W, LR, and NS.

*continued...*

**Terminal Injection Site Compatibility:** Dex/AA solutions. Aminophylline, amiodarone, aztreonam, caffeine citrate, calcium chloride, caspofungin, cefotaxime, cefoxitin, ceftazidime, chloramphenicol, dobutamine, enalaprilat, epinephrine, esmolol, famotidine, fentanyl, fluconazole, flumazenil, gentamicin, heparin, hydrocortisone succinate, ibuprofen lysine, lidocaine, linezolid, lorazepam, meropenem, metronidazole, micafungin, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, oxacillin, pancuronium bromide, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E<sub>1</sub>, ranitidine, tobramycin, vecuronium, and zidovudine.

**Incompatibility:** Acyclovir, alteplase, amphotericin B, ampicillin, cefepime, furosemide, indomethacin, insulin, penicillin G, and sodium bicarbonate.

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Compatibilities updated 10/2009

Adverse Effects/Precautions updated 1/2009

Special Considerations and References updated 3/2008

**Dose & Administration**

Begin with 40 mcg/kg per dose (0.04 mg/kg per dose) given orally every 24 hours. Usual maximum dose 150 mcg/kg per dose (0.15 mg/kg per dose), as frequently as every 6 hours. Titrate subsequent doses and interval based on amount and duration of response. Dosage may need to be increased every few days.

**Uses**

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

**Monitoring**

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

**Adverse Effects/Precautions**

Use with extreme caution in patients with impaired renal function: oliguria and increased serum creatinine occur frequently. Hypotension occurs primarily in patients who are volume-depleted. Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements. Cough has been reported frequently in adults.

**Pharmacology**

Enalapril is a prodrug that is hydrolyzed in the liver to form the active angiotensin-converting enzyme (ACE) inhibitor enalaprilat, which blocks the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Enalaprilat also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Bioavailability of oral dosage form is uncertain in neonates, but is significantly less than the 60% reported in adults. Onset of action after oral dose is 1 to 2 hours. Duration of action is quite variable in neonates, ranging from 8 to 24 hours.

**Special Considerations/Preparation**

Supplied in 2.5-mg, 5-mg, 10-mg, and 20-mg tablets. Enalapril oral suspension (200 mL total) can be prepared by crushing ten 20-mg tablets and adding 50 mL of isotonic citrate buffer (Bicitra®). Mixture should be placed in a bottle and shaken for at least 2 minutes, left to stand for 60 minutes, and then shaken for an additional minute. Add 150 mL of Ora-Sweet<sup>SM</sup>, yielding a final concentration of 1 mg/mL. Suspension is stable for 30 days refrigerated.

**Selected References**

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- ◆ Wells TG, Bunchman TE, Kearns GL: Treatment of neonatal hypertension with enalaprilat. *J Pediatr* 1990;117:665.
- ◆ Frenneaux M, Stewart RAH, Newman CMH, Hallidie-Smith KA: Enalapril for severe heart failure in infancy. *Arch Dis Child* 1989;64:219.
- ◆ Product Information, BTA Pharmaceuticals, Inc., 2008.

Special Considerations and References updated 12/2010

Text updated 3/1997



**Dose & Administration**

Begin with 10 mcg/kg per dose (0.01 mg/kg per dose) IV over 5 minutes every 24 hours. Titrate subsequent doses and interval based on amount and duration of response. Dosage may need to be increased every few days.

**Uses**

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

**Monitoring**

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

**Adverse Effects/Precautions**

Use with extreme caution in patients with impaired renal function: oliguria and increased serum creatinine occur frequently. Hypotension occurs primarily in patients who are volume-depleted. Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements. Cough has been reported frequently in adults.

**Pharmacology**

Enalaprilat is an ACE inhibitor which blocks the production of the potent vasoconstrictor angiotensin II. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Enalaprilat also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Duration of action is quite variable in neonates, ranging from 8 to 24 hours.

**Special Considerations/Preparation**

Enalaprilat is supplied as a 1.25 mg/mL solution for injection in 1 mL and 2 mL vials. Benzyl alcohol content is 9 mg/mL. To make a dilution for IV use, take 1 mL (1.25 mg) of solution and add 49 mL NS to make a final concentration of 25 mcg/mL (0.025 mg/mL). Dilution stable for 24 hours.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>5</sub>NS, and NS.

**Terminal Injection Site Compatibility:** Amikacin, aminophylline, ampicillin, aztreonam, calcium gluconate, cefazolin, ceftazidime, chloramphenicol, cimetidine, clindamycin, dobutamine, dopamine, erythromycin lactobionate, esmolol, famotidine, fentanyl, gentamicin, heparin, hydrocortisone succinate, lidocaine, linezolid, magnesium sulfate, meropenem, metronidazole, morphine, nafcillin, nicardipine, nitroprusside, penicillin G, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanyl, tobramycin, trimethoprim-sulfamethoxazole, and vancomycin.

**Incompatibility:** Amphotericin B, cefepime, and phenytoin.

*continued...*

**Selected References**

- ♦ Schilder JLAM, Van den Anker JN: Use of enalapril in neonatal hypertension. *Acta Paediatr* 1995;84:1426.
- ♦ Mason T, Polak MJ, Pyles L, et al: Treatment of neonatal renovascular hypertension with intravenous enalapril. *Am J Perinatol* 1992;9:254.
- ♦ Rasoulpour M, Marinelli KA: Systemic hypertension. *Clin Perinatol* 1992;19:121.
- ♦ Wells TG, Bunchman TE, Kearns GL: Treatment of neonatal hypertension with enalaprilat. *J Pediatr* 1990;117:665.
- ♦ Frenneaux M, Stewart RAH, Newman CMH, Hallidie-Smith KA: Enalapril for severe heart failure in infancy. *Arch Dis Child* 1989;64:219.
- ♦ Product Information, Hospira, 2006.

Compatibilities updated 7/2009

Text updated 3/2008

**Dose & Administration****Initial treatment of thrombosis:**

Term infants: 1.7 mg/kg per dose subQ every 12 hours.

Preterm infants: 2 mg/kg per dose subQ every 12 hours.

Adjust dosage to maintain anti-factor  $X_a$  level between 0.5 and 1.0 unit/mL. It will usually take several days to attain levels in the target range.

Dosage requirements to maintain target anti-factor  $X_a$  levels in preterm infants are quite variable, ranging from 0.8 to 3 mg/kg every 12 hours. Infants older than 3 months of age: 1 mg/kg per dose subQ every 12 hours.

Call 1-800-NOCLOTS for case reporting and treatment guidance.

In a retrospective study, whole-milligram enoxaparin dosing using insulin syringes (undiluted 100 mg/mL; 1 mg enoxaparin = 0.01 mL = 1 unit) was associated with therapeutic anti- $X_a$  levels and no reported dose measurement errors. The study included neonates, infants and children ( $n=514$ ); 27% were infants less than 3 months of age (900 to 4700 g in weight). Five children (less than 1%) had a supra-therapeutic initial anti- $X_a$  level without hemorrhagic consequences. No patients needed decimal dosing to attain therapeutic levels.

**Low-risk prophylaxis:** 0.75 mg/kg per dose subQ every 12 hours.

Infants older than 3 months of age: 0.5 mg/kg per dose subQ every 12 hours.

Adjust dosage to maintain anti-factor  $X_a$  level between 0.1 and 0.4 units/mL.

Administration may be aided by using a small plastic indwelling subcutaneous catheter (Insuflon®, Hypoguard USA). Adverse events related to these catheters are much more frequent in ELBW infants.

**Uses**

Anticoagulation. Advantages over standard unfractionated heparin: (1) may be given subcutaneously, (2) more predictable pharmacokinetics, (3) dosing every 8 to 12 hours, (4) less frequent bleeding complications.

**Monitoring**

Measure anti-factor  $X_a$  concentrations 4 hours after a dose (See above for desired range). Preterm infants are likely to require several dosage adjustments to achieve the target levels. After attaining target levels, dosage adjustments will be necessary once or twice a month, perhaps more often in preterm infants and infants with hepatic or renal dysfunction. Assess for signs of bleeding and thrombosis.

*continued...*

**Adverse Effects/Precautions****Black Box Warning**

Epidural or spinal hematomas, which may result in long-term or permanent paralysis, may occur in patients who are anticoagulated with low molecular weight heparins or heparinoids and are receiving neuraxial anesthesia or undergoing spinal puncture. Factors that can increase the risk of developing these hematomas include: use of indwelling epidural catheters, concomitant use of drugs affecting hemostasis such as NSAIDs, platelet inhibitors, or other anticoagulants, or history of traumatic or repeated epidural or spinal puncture, spinal deformity, or spinal surgery. Monitor patients frequently for neurological impairment. If neurological compromise is noted, urgent treatment is necessary. Consider risks/benefits before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

Major bleeding may occur even with anti-factor X<sub>a</sub> levels in the therapeutic range. The overall incidence is approximately 4%. Reported complications include major bleeding or hematoma at the administration site, compartment syndrome, intracranial hemorrhage, and gastrointestinal hemorrhage.

**Pharmacology**

Enoxaparin is a low-molecular weight heparin that has considerably less activity against thrombin than does standard heparin. Efficacy in neonates is decreased due to low antithrombin plasma concentrations. It is also much less likely to interfere with platelet function or cause osteoporosis. It activates antithrombin III, which progressively inactivates both thrombin and factor X<sub>a</sub>, key proteolytic enzymes in the formation of fibrinogen and activation of prothrombin. Bioavailability is almost 100% after subcutaneous administration, with peak activity 2.5 to 4 hours later. The apparent half-life of anti-X<sub>a</sub> activity is 4 to 5 hours. Clearance in neonates is more rapid than in older infants, children or adults.

**Special Considerations/Preparation**

Available as 100 mg/mL concentration as 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/mL in preservative-free prefilled syringes. Multidose vial available in 100 mg/mL concentration with 15 mg benzyl alcohol per 1 mL as a preservative.

A 20-mg/mL enoxaparin dilution (in preservative-free sterile water) was stable for 4 weeks in glass vials stored at room temperature. The same dilution was stable in 1-mL tuberculin syringes (6 mg/0.3 mL) for 2 weeks stored at room temperature or under refrigeration. The stability end-point was significant loss of anti-X<sub>a</sub> activity; sterility and pyrogenicity tests were not performed.

**Solution Compatibility:** NS and sterile water.

*continued...*

## Selected References

- ◆ Bauman ME, Black KL, Bauman ML, et al: Novel uses of insulin syringes to reduce dosing errors: A retrospective chart review of enoxaparin whole milligram dosing. *Thromb Res* 2009;123:845-847.
- ◆ Dager WE, Gosselin RC, King JH, et al: Anti-Xa stability of diluted enoxaparin for use in pediatrics. *Ann Pharmacother* 2004;38:569-573.
- ◆ Malowany JJ, Monagle P, Knoppert DC, et al: Enoxaparin for neonatal thrombosis: a call for a higher dose in neonates. *Thrombosis Research* 2008;122:826-830.
- ◆ Monagle P, Chalmers E, Chan A, et al: Antithrombotic therapy in neonates and children: Antithrombotic and thrombolytic therapy, 8th Ed. *Chest* 2008;133:887S-968S.
- ◆ Malowany JJ, Knoppert DC, Chan AKC, et al: Enoxaparin use in the neonatal intensive care unit: experience over 8 years. *Pharmacotherapy* 2007;27:1263-1271.
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- ◆ Dunaway KK, Gal P, Ransom JL: Use of enoxaparin in a preterm infant. *Ann Pharmacother* 2000;34:1410-3.
- ◆ Klinger G, Hellmann J, Daneman A: Severe aortic thrombosis in the neonate - successful treatment with low-molecular-weight heparin: Two case reports and review of the literature. *Am J Perinatol* 2000;17:151-8.
- ◆ Product Information, Sanofi-Aventis, 2009.

Dose & Administration, Special Considerations, and References updated 2/2011

Adverse Effects/Precautions and References updated 12/2010



**Dose & Administration**

**Resuscitation and severe bradycardia:** 0.1 to 0.3 mL/kg 1:10,000 concentration; equal to 0.01 to 0.03 mg/kg (10 to 30 mcg/kg). IV push, or IC.

When using the endotracheal route, consider a higher dose, 0.05 to 0.1 mg/kg (50 to 100 mcg/kg) ET, immediately followed by 1 mL NS. Do **not** administer these higher doses of epinephrine intravenously.

**IV continuous infusion:** Start at 0.1 mcg/kg per minute and adjust to desired response, to a maximum of 1 mcg/kg per minute. If possible, correct acidosis before administration of epinephrine to enhance the effectiveness of the drug.

**Solution Preparation Calculations**

To calculate the **AMOUNT** of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the **VOLUME** of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

**Example (for Epinephrine):** Mix 50 mL of 20 mcg/mL solution using epinephrine concentration of 1 mg/mL.

20 mcg/mL = 0.02 mg/mL

0.02 mg/mL x 50 mL = 1 mg epinephrine

$$\frac{\text{*1 mg}}{\text{1 mg/mL}} = \text{1 mL of epinephrine}$$

Add 1 mL of epinephrine (1:1000) to 49 mL of compatible solution (eg, D<sub>5</sub> W) to yield 50 mL of infusion solution with a concentration of 20 mcg/mL.

**Maximum concentration 60 mcg/mL.**

*continued...*

Epinephrine Titration Chart 

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
10	0.05	0.3
	0.1	0.6
	0.5	3
	1	6
20	0.05	0.15
	0.1	0.3
	0.5	1.5
	1	3
30	0.05	0.1
	0.1	0.2
	0.5	1
	1	2
40	0.05	0.075
	0.1	0.15
	0.5	0.75
	1	1.5
50	0.05	0.06
	0.1	0.12
	0.5	0.6
	1	1.2
60	0.05	0.05
	0.1	0.1
	0.5	0.5
	1	1

**Uses**

Acute cardiovascular collapse. Short-term use for treatment of systemic hypotension. Despite the widespread use of epinephrine/adrenaline during resuscitation, no placebo-controlled studies have evaluated either the tracheal or intravenous administration of epinephrine at any stage during cardiac arrest in human neonates. Nonetheless, it is reasonable to continue to use epinephrine when adequate ventilation and chest compressions have failed to increase the heart rate to greater than 60 beats per minute.

**Monitoring**

Monitor heart rate and blood pressure continuously. Observe IV site for signs of infiltration.

**Adverse Effects/Precautions**

Compared to dopamine, continuous infusions at doses yielding similar changes in blood pressure are more likely to cause hyperglycemia, tachycardia, and elevations in serum lactate. Cardiac arrhythmias (PVCs and ventricular tachycardia) are also more likely. Renal vascular ischemia may occur at higher doses. Bolus doses are associated with severe hypertension and intracranial hemorrhage. Increased myocardial oxygen requirements.

IV infiltration may cause tissue ischemia and necrosis. Suggested treatment: Inject a 1 mg/mL solution of phentolamine into the affected area. The usual amount needed is 1 to 5 mL, depending on the size of the infiltrate.

*continued...*



### Pharmacology

Epinephrine (adrenaline) is the major hormone secreted by the adrenal medulla. It is a potent stimulator of both alpha and beta adrenergic receptors, with complex effects on body organ systems. Low doses are associated with systemic and pulmonary vasodilation. Higher doses increase blood pressure by direct myocardial stimulation, increases in heart rate, and vasoconstriction. Myocardial oxygen consumption is increased. Blood flow to skeletal muscle, brain, liver, and myocardium is increased. However, blood flow to the kidney is decreased due to increased vascular resistance.

### Special Considerations/Preparation

Always use as a 1:10,000 concentration (0.1 mg/mL) for individual doses.

Use 1:1000 (1 mg/mL) concentration to prepare continuous infusion solution.

Protect from light.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Amikacin, amiodarone, caffeine citrate, calcium chloride, calcium gluconate, ceftazidime, cimetidine, dobutamine, dopamine, famotidine, fentanyl, furosemide, heparin, hydrocortisone succinate, ibuprofen lysine, lorazepam, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanyl, vecuronium, and vitamin K<sub>1</sub>.

**Incompatibility:** Aminophylline, ampicillin, hyaluronidase, micafungin, and sodium bicarbonate.

### Selected References

- ◆ Perlman JM, Wyllie J, Kattwinkel J, et al on behalf of the Neonatal Resuscitation Chapter Collaborators. Part 11: Neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2010;122(suppl 2):S516-S538.
- ◆ Barber CA, Wyckoff MH: Use and efficacy of endotracheal versus intravenous epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *Pediatrics* 2006;118:1028-1034.
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URL: <http://www.pediatrics.org/cgi/content/full/117/6/e1213>.
- ◆ Pellicer A, Valverde E, Elorza MD, et al: Cardiovascular support for low birth weight infants and cerebral hemodynamics: a randomized, blinded clinical trial. *Pediatrics* 2005; 115: 1501-1512.
- ◆ Burchfield DJ: Medication use in neonatal resuscitation. *Clin Perinatol* 1999;26:683-691.

Dose & Administration and References updated 12/2010

Compatibilities updated 10/2009

Updated 03/2008



**Dose & Administration****Starting IV doses:**

**Supraventricular tachycardia (SVT):** 100 mcg/kg per minute continuous infusion. Increase in increments of 50 to 100 mcg/kg per minute every 5 minutes until control of the ventricular rate is achieved.

**Acute management of postoperative hypertension:** 50 mcg/kg per minute continuous infusion. Increase in increments of 25 to 50 mcg/kg per minute every 5 minutes until desired blood pressure is achieved.

**Usual maximum dosage:** 200 mcg/kg per minute.

Doses greater than 300 mcg/kg per minute are likely to cause hypotension.

**Uses**

Short term treatment of postoperative hypertension, supraventricular tachycardia (SVT), and ventricular tachycardia (VT).

**Monitoring**

Continuous EKG monitoring during acute treatment of arrhythmias. Measure systemic blood pressure and heart rate frequently.

**Adverse Effects/Precautions**

May cause hypotension in high doses. Adverse effects reversible with discontinuation of drug. Monitor IV site closely for vein irritation and phlebitis, especially at high concentrations (greater than 10 mg/mL).

**Pharmacology**

Esmolol is a potent cardio-selective beta-blocking agent with a uniquely short half-life (2.8 to 4.5 minutes) and a brief (10 to 15 minute) duration of action. There appears to be no correlation between age and pharmacodynamic response or pharmacokinetic profile. Esmolol is cleared primarily by red blood cell esterases. Renal or hepatic failure does not effect elimination.

**Special Considerations/Preparation**

Esmolol is supplied in preservative-free 10-mL (10 mg/mL) vials, and 2500 mg/250 mL and 2000 mg/100 mL ready-to-use premixed bags. The pH is approximately 4.5 to 5.5. Osmolarity is 312 mOsm/L. Store at room temperature. Stable for at least 24 hours at room temperature or refrigeration when diluted in compatible solutions to a concentration of 10 mg/mL.

**Solution Compatibility:** D<sub>5</sub>W, LR, D<sub>5</sub>LR, NS, ½ NS, D<sub>5</sub> ½ NS, and D<sub>5</sub>NS.

**Terminal Injection Site Compatibility:** Amikacin, aminophylline, atracurium, calcium chloride, cefazolin, ceftazidime, chloramphenicol, cimetidine, clindamycin, dopamine, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, gentamicin, heparin, hydrocortisone, insulin, linezolid, magnesium sulfate, metronidazole, micafungin, midazolam, morphine, nafcillin, nicardipine, nitroglycerin, norepinephrine, pancuronium, penicillin G, phenytoin, piperacillin, potassium chloride, propofol, ranitidine, remifentanyl, sodium nitroprusside, tobramycin, trimethoprim/sulfamethoxazole, vancomycin, and vecuronium.

**Incompatibility:** Amphotericin B, diazepam, furosemide, and procainamide.

*continued...*

**Selected References**

- ◆ Wiest DB, Garner SS, Uber WE, et al: Esmolol for the management of pediatric hypertension after cardiac operations. *J Thoracic Cardiovas Surg* 1998;115:890-897.
- ◆ Cuneo B, Zales VR, Blahunka PC, et al: Pharmacodynamics and pharmacokinetics of esmolol, a short-acting  $\beta$ -blocking agent, in children. *Pediatr Cardiol* 1994;15:296-301.
- ◆ Trippel MD, Wiest DB, Gillette PC: Cardiovascular and antiarrhythmic effects of esmolol in children. *J Pediatr* 1991;119:142-147.
- ◆ Wiest DB, Trippel MD, Gillette PC, et al: Pharmacokinetics of esmolol in children. *Clin Pharmacol Ther* 1991;49:618-623.
- ◆ Product Information, Baxter, 2007.

Special Considerations and Compatibilities updated 12/2010

Dose updated 3/2007

Added 3/2006

**Dose & Administration**

Begin at 2 mg/kg per dose every 12 hours orally. Adjust dose based on response and serum concentrations to a maximum of 4 mg/kg per dose every 12 hours. Correct preexisting hypokalemia or hyperkalemia before administration. Optimal effect may take 2 to 3 days of therapy to achieve, and steady-state plasma levels may not be reached until 3 to 5 days at a given dosage in patients with normal renal and hepatic function. Therefore, do not increase dosage more frequently than approximately once every 4 days.

**Uses**

Treatment of supraventricular arrhythmias not responsive to conventional therapies. Contraindicated in patients with structurally abnormal hearts.

**Monitoring**

Continuous EKG during initiation of therapy, as this is the most common time to see drug-induced arrhythmias. Follow trough serum concentrations closely at initiation, 3 to 5 days after any dose change, and with any significant change in clinical status or diet. Therapeutic trough levels are 200 to 800 nanograms/mL.

**Adverse Effects/Precautions****Black Box Warning**

An excessive mortality or non-fatal cardiac arrest rate was seen in patients (adults) with asymptomatic non-life-threatening ventricular arrhythmias and a history of myocardial infarction treated with flecainide compared with that seen in patients assigned to a carefully matched placebo-treated group in the Cardiac Arrhythmia Suppression Trial (CAST). It is prudent to consider the risks of Class IC agents (including flecainide), coupled with the lack of any evidence of improved survival, generally unacceptable in patients without life-threatening ventricular arrhythmias, even if the patients are experiencing unpleasant, but not life-threatening, symptoms or signs. Flecainide is not recommended for use in patients with chronic atrial fibrillation. Case reports of ventricular proarrhythmic effects in patients treated with flecainide for atrial fibrillation/flutter have included increased PVCs, VT, ventricular fibrillation (VF), and death.

Flecainide can cause new or worsened arrhythmias, including AV block, bradycardia, ventricular tachycardia, torsades de pointes. There is also a negative inotropic effect. Dizziness, blurred vision, and headache have been reported in children.

**Pharmacology**

Flecainide is a Class I-C antiarrhythmic that produces a dose-related decrease in intracardiac conduction in all parts of the heart, thereby increasing PR, QRS and QT intervals. Effects upon atrioventricular (AV) nodal conduction time and intra-atrial conduction times are less pronounced than those on the ventricle. Peak serum concentrations occur 2 to 3 hours after an oral dose. Infant formula and milk products interfere with drug absorption. Plasma protein binding is about 40% in adults and is independent of plasma drug level. Children under 1 year of age have elimination half-life values of 11 to 12 hours. Elimination half-life in newborns after maternal administration is as long as 29 hours.

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**Special Considerations/Preparation**

Supplied in 50-mg, 100-mg, and 150-mg tablets. An oral suspension with a final concentration of 5 mg/mL can be made as follows: crush 6 (six) 100-mg tablets, slowly mix in 20 mL of a 1:1 mixture of Ora-Sweet® and Ora-Plus®, or cherry syrup (cherry syrup concentrate diluted 1:4 with simple syrup) to form a uniform paste, then add to this mixture enough vehicle to make a final volume of 120 mL. Shake well and protect from light. Stable for 45 days refrigerated and at room temperature when stored in amber glass or plastic.

An oral suspension with a final concentration of 20 mg/mL may also be compounded. Extemporaneously compounded flecainide acetate 20 mg/mL prepared in either a 1:1 mixture of Ora-Sweet® and Ora-Plus®, a 1:1 mixture of Ora-Sweet SF® and Ora-Plus®, or cherry syrup (cherry syrup concentrate diluted 1:4 with simple syrup) and placed in a 120-mL amber polyethylene terephthalate bottle is stable, retaining a mean of at least 92% of the initial drug concentration, for up to 60 days when stored without light at 5 and 25 degrees C.

**Selected References**

- ◆ Allen LV Jr & Erickson MA III: Stability of baclofen, captopril, diltiazem hydrochloride, dipyrindamole, and flecainide acetate in extemporaneously compounded oral liquids. *Am J Health-Syst Pharm* 1996;53:2179-2184.
- ◆ O'Sullivan JJ, Gardiner HM, Wren C: Digoxin or flecainide for prophylaxis of supraventricular tachycardia in infants? *J Am Coll Cardiol* 1995;26:991-994.
- ◆ Luedtke SA, Kuhn RJ, McCaffrey FM: Pharmacologic management of supraventricular tachycardia in children. *Ann Pharmacother* 1997;31:1227-43.
- ◆ Perry JC, Garson A: Flecainide acetate for treatment of tachyarrhythmias in children: Review of world literature on efficacy, safety, and dosing. *Am Heart J* 1992;124:1614-21.
- ◆ Wiest DB, Garner SS, Pagacz LR, et al: Stability of flecainide acetate in an extemporaneously compounded oral suspension. *Am J Hosp Pharm* 1992;49:1467-70.

Adverse Effects/Precautions, Special Considerations and References  
updated 12/2010  
Added 3/2003

### Dose & Administration

**Maintaining patency of peripheral and central vascular catheters:**  
0.5 to 1 unit/mL of IV fluid.

**Treatment of thrombosis:** 75 units/kg bolus over 10 minutes, followed by 28 units/kg per hour continuous infusion. Four hours after initiating therapy, measure aPTT, then adjust dose to achieve an aPTT that corresponds to an anti-factor  $X_a$  level of 0.35 to 0.7 (this is usually equivalent to an aPTT of 60 to 85 seconds). Treatment should be limited to 10 to 14 days. Some experts recommend switching to low molecular weight heparin after 3 to 5 days.

**Make certain correct concentration is used.**

Effective October 1, 2009, a revised United States Pharmacopeia (USP) reference standard and test method has resulted in approximately 10% reduction in heparin potency per USP unit. It is unlikely that the change in potency will have clinical significance. Clinicians should be aware of this change in potency in the event that there are any differences in response to heparin therapy in practice. Manufacturers will provide an identifier (an 'N' next to the lot number) on heparin products made under the new USP standards.

### Uses

See above. Only continuous infusions (rather than intermittent flushes) have been demonstrated to maintain catheter patency. Treatment of renal vein thromboses is limited to those that are bilateral or extend into the IVC. Although data are limited, enoxaparin may be preferable to heparin for treatment of thromboses.

Call 1-800-NOCLOTS for case reporting and treatment guidance.

### Monitoring

Follow platelet counts every 2 to 3 days. When treating thromboses, maintain a prolonged aPTT in a range corresponding to an anti-factor  $X_a$  level of 0.3 to 0.7 units/mL (usually equivalent to an aPTT of 60 to 85 seconds). Assess for signs of bleeding and thrombosis.

### Adverse Effects/Precautions

Data are insufficient to make specific recommendations regarding anticoagulation therapy. Heparin-induced thrombocytopenia (HIT) has been reported to occur in approximately 1% of newborns exposed to heparin. Heparin-associated antiplatelet antibodies were found in half of the newborns who were both thrombocytopenic and heparin-exposed. Although the thrombocytopenia resolved spontaneously in most patients upon stopping the heparin, a high incidence of ultrasonographic-documented aortic thrombosis was seen. Contraindicated in infants with evidence of intracranial or GI bleeding or thrombocytopenia (below 50,000/mm<sup>3</sup>). Long term use of therapeutic doses of heparin can lead to osteoporosis. Confirm heparin vial concentration prior to administration of the drug. Fatal hemorrhages have occurred in pediatric patients when the incorrect heparin concentration was administered.

*continued...*

**Pharmacology**

Activates antithrombin III, which progressively inactivates both thrombin and factor X<sub>a</sub>, key proteolytic enzymes in the formation of fibrinogen and activation of prothrombin. Efficacy in neonates is decreased due to low antithrombin plasma concentrations. Metabolized by liver. Renal excretion should occur within 6 hours, but may be delayed. Clearance in neonates is more rapid than in children or adults. Half-life is dose-dependent, but averages 1 to 3 hours.

**Special Considerations/Preparation**

**Keep protamine sulfate on hand to manage hemorrhage (see Protamine monograph for appropriate dosing).**

Heparin available in 10 units/mL (for IV reservoirs); 100 units/mL; 1000 units/mL (for central catheters); 5000 units/mL, 10,000 units/mL, and 20,000 units/mL. Also available in premixed infusion bags in D<sub>5</sub>W, NS, and ½ NS in various concentrations.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, NS, and 1/2NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, aminophylline, amphotericin B, ampicillin, atropine, aztreonam, caffeine citrate, calcium gluconate, cefazolin, cefepime, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, flumazenil, furosemide, micafungin, hydralazine, hydrocortisone succinate, ibuprofen lysine, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, metronidazole, midazolam, milrinone, morphine, nafcillin, naloxone, neostigmine, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenobarbital, phytonadione, piperacillin, piperacillin-tazobactam, potassium chloride, procainamide, propofol, propranolol, ranitidine, remifentanyl, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, trimethoprim-sulfamethoxazole, vecuronium, and zidovudine.

**Incompatibility:** Alteplase, amikacin, amiodarone, caspofungin, diazepam, gentamicin, hyaluronidase, methadone, netilmicin, phenytoin, tobramycin, and vancomycin.

*continued...*



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- ◆ Product Information, Abraxis, 2008.

Special Considerations and Compatibilities updated 12/2010  
 Dose & Administration and References updated 7/2010  
 Adverse Effects/Precautions updated 1/2009



**Dose & Administration**

**IV:** Begin with 0.1 to 0.5 mg/kg per dose every 6 to 8 hours. Dose may be gradually increased as required for blood pressure control to a maximum of 2 mg/kg per dose every 6 hours.

**Oral:** 0.25 to 1 mg/kg per dose every 6 to 8 hours, or approximately twice the required IV dose. Administer with food to enhance absorption.

**Note:** Use with a beta-blocking agent is often recommended to enhance the antihypertensive effect and decrease the magnitude of the reflex tachycardia. This is expected to reduce hydralazine IV dosage requirements to less than 0.15 mg/kg per dose.

**Uses**

Treatment of mild to moderate neonatal hypertension by vasodilation. Afterload reduction in patients with congestive heart failure.

**Monitoring**

Frequent assessment of blood pressure and heart rate. Guaiac stools. Periodic CBC during long-term use.

**Adverse Effects/Precautions**

Diarrhea, emesis, and temporary agranulocytosis have been reported in neonates. Tachycardia, postural hypotension, headache, nausea, and a lupus-like syndrome occur in 10% to 20% of adults. Uncommon reactions in adults include GI irritation and bleeding, drug fever, rash, conjunctivitis, and bone marrow suppression.

**Pharmacology**

Causes direct relaxation of smooth muscle in the arteriolar resistance vessels. Major hemodynamic effects: Decrease in systemic vascular resistance and a resultant increase in cardiac output. Increases renal, coronary, cerebral, and splanchnic blood flow. When administered orally, hydralazine has low bioavailability because of extensive first-pass metabolism by the liver and intestines. The rate of enzymatic metabolism is genetically determined by the acetylator phenotype—slow acetylators have higher plasma concentrations and a higher incidence of adverse effects.

**Special Considerations/Preparation**

Hydralazine hydrochloride injection for IV use (20 mg/mL) is available in 1 mL vial. A 1 mg/mL dilution may be made by diluting 0.5 mL of the 20 mg/mL concentrate with 9.5 mL of preservative-free normal saline for injection. Dilution is stable for 24 hours.

Oral tablet strengths include 10-, 25-, 50-, and 100-mg. Oral formulations using simple syrups containing dextrose, fructose, or sucrose are unstable. To prepare an oral suspension, crush a 50 mg tablet and dissolve in 4 mL of 5% mannitol, then add 46 mL of sterile water to make a final concentration of 1 mg/mL. Protect from light. Stable for 7 days refrigerated.

**Solution Compatibility:** NS.

**Terminal Injection Site Compatibility:** Dobutamine, heparin, hydrocortisone succinate, and potassium chloride.

**Incompatibility:** Aminophylline, ampicillin, diazoxide, furosemide, and phenobarbital.

*continued...*

**Selected References**

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- ◆ Product Information, American Regent, 2003.

Compatibilities updated 7/2009

Text updated 3/1996

**Dose & Administration**

**First dose:** 10 mg/kg.

**Second and third doses:** 5 mg/kg.

Administer IV by syringe pump over 15 minutes at 24 hour intervals.

**Uses**

Closure of Patent Ductus Arteriosus. Not indicated for IVH prophylaxis.

**Monitoring**

Assess for ductal closure. Monitor urine output. Assess for signs of bleeding.

**Adverse Effects/Precautions**

NeoProfen® is contraindicated in preterm neonates with 1) infection, 2) active bleeding, 3) thrombocytopenia or coagulation defects, 4) NEC, 5) significant renal dysfunction, and 6) congenital heart disease with ductal-dependent systemic blood flow. Decreased urine output is less severe and occurs less frequently than with indomethacin. Although the available (and few) data suggest that the displacement of bilirubin from albumin is minimal with an ibuprofen dosing regimen of 10-, 5-, 5-mg/kg (every 24 hr), a more significant increase in unbound bilirubin can be expected in those infants with a high unconjugated bilirubin/albumin ratio and those in whom high ibuprofen concentrations are achieved. There is one recent case report of pulmonary hypertension in a 32 week gestation infant in Italy who received ibuprofen lysine (not NeoProfen) for treatment of PDA. Several studies have demonstrated an increased risk of oxygen dependency at 28 days postnatal age, but not 36 weeks PMA. Ibuprofen, like other nonsteroidal anti-inflammatory drugs, can inhibit platelet aggregation.

**Pharmacology**

NeoProfen® is a lysine salt solution of racemic ibuprofen, an inhibitor of prostaglandin synthesis. In adults (no data in neonates) metabolism is primarily via hydroxylation by hepatic CYP 2C9 and 2C8, with renal elimination of unchanged drug (10% to 15%) and metabolites. The mean half-life in premature neonates is approximately 43 hours, with large interpatient variability. Clearance increases rapidly with postnatal age and PDA closure.

**Special Considerations/Preparation**

Supplied as a 10 mg/mL sterile solution for injection in 2 mL single use vials. Should be diluted prior to administration in an appropriate volume of dextrose or saline. Contains no preservatives and is not buffered. Administer within 30 minutes of preparation. The pH is adjusted to 7. Store at room temperature. **Protect from light.**

**Solution Compatibility:** NS and D5W.

**Terminal Injection Site Compatibility:** Cefazidime, dopamine, epinephrine, furosemide, heparin, insulin, morphine, phenobarbital, potassium chloride, sodium bicarbonate.

**Incompatibility:** Dex/AA. Caffeine citrate, dobutamine, and vecuronium.

*continued...*

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- ◆ Ambat MT, Ostrea EM Jr, Aranda JV: Effect of ibuprofen L-lysinate on bilirubin binding to albumin as measured by saturation index and horseradish peroxidase assays. *J Perinatol* 2008;28:287-90.
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- ◆ Lundbeck Inc.: Compatibility data on file as of October 2009.
- ◆ Product Information, Lundbeck Inc., 2009

Compatibilities updated 10/2009

Adverse Effects and References updated 3/2007

**Dose & Administration**

IV infusion by syringe pump over at least 30 minutes to minimize adverse effects on cerebral, GI, and renal blood flow velocities. Usually three doses per course, maximum two courses. Give at 12- to 24-hour intervals with close monitoring of urine output. If anuria or severe oliguria occurs, subsequent doses should be delayed.

Longer treatment courses may be used: 0.2 mg/kg every 24 hours for a total of 5 to 7 days.

**Prevention of IVH:** 0.1 mg/kg every 24 hours for 3 doses, beginning at 6 to 12 hours of age.

**PDA Closure Dose (mg/kg)**

Age at 1st dose	1st	2nd	3rd
< 48 h	0.2	0.1	0.1
2 to 7 d	0.2	0.2	0.2
> 7 d	0.2	0.25	0.25

**Uses**

Closure of ductus arteriosus. Prevention of intraventricular hemorrhage.

**Monitoring**

Monitor urine output, serum electrolytes, glucose, creatinine and BUN, and platelet counts. Assess murmur, pulse pressure. Assess for gastrointestinal bleeding by gastric and fecal occult blood testing. Observe for prolonged bleeding from puncture sites.

**Adverse Effects/Precautions**

Contraindicated in active bleeding, significant thrombocytopenia or coagulation defects, necrotizing enterocolitis, and/or significantly impaired renal function. If oliguria occurs, observe for hyponatremia and hypokalemia, and consider prolonging the dosing interval of renally excreted drugs (eg, gentamicin). Consider withholding feedings. Concomitant therapy with furosemide may lead to increased hyponatremia and a significant rise in serum creatinine. Hypoglycemia is common, usually preventable by increasing the glucose infusion rate by 2 mg/kg per minute. Causes platelet dysfunction. Rapid (less than 5-minute) infusions are associated with reductions in organ blood flow. Gastrointestinal perforations occur frequently if used concurrently with corticosteroids.

**Pharmacology**

Inhibitor of prostaglandin synthesis. Decreases cerebral, renal and GI blood flow. Metabolized in the liver to inactive compounds and excreted in the urine and feces. Serum half-life is approximately 30 hours, with a range of 15 to 50 hours, partially dependent on postnatal age. In most studies, the response of the ductus and adverse effects of indomethacin are only weakly correlated with plasma concentration.

**Special Considerations/Preparation**

Supplied as a lyophilized powder in 1-mg single dose vials. Indomethacin sodium trihydrate salt is not buffered, and is insoluble in solutions with pH less than 6; the manufacturer therefore recommends against continuous infusion in typical IV solutions. Reconstitute using 1 to 2 mL of preservative-free NS or sterile water for injection. Reconstituted indomethacin is stable in polypropylene syringes and glass vials for 12 days when stored at room temperature or refrigerated. Observe for precipitation.

*continued...*

**Solution Compatibility:** Sterile water for injection.

(No visual precipitation in 24 hours): D<sub>2.5</sub>W, D<sub>5</sub>W, and NS.

**Solution Incompatibility:** D7.5W, D10W, and Dex/AA Solutions.

**Terminal Injection Site Compatibility:** Furosemide, insulin, nitroprusside, potassium chloride, and sodium bicarbonate.

**Incompatibility:** Calcium gluconate, cimetidine, dobutamine, dopamine, gentamicin, and, tobramycin.

### Selected References

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- ◆ Schmidt B, Davis P, Moddemann D, et al: Long-term effects of indomethacin prophylaxis in extremely-low-birth-weight infants. *N Engl J Med* 2001; 344:1966-1972.
- ◆ Ment LR, Oh W, Ehrenkranz RA, et al: Low-dose indomethacin and prevention of intraventricular hemorrhage: A multicenter randomized trial. *Pediatrics* 1994;93:543.
- ◆ Product Information, Ovation Pharmaceuticals, 2006.

Adverse Effect/Precautions and References updated 2/2011

Compatibilities updated 7/2009

References updated 3/2004



**Dose & Administration**

0.05 to 0.5 mcg/kg per minute continuous IV infusion.

Maximum dose 2 mcg/kg per minute.

Dosage often titrated according to heart rate.

Acidosis should be corrected before infusion.

**Solution Preparation Calculations**

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

**Example (for Isoproterenol):** Mix 50 mL of 10 mcg/mL solution using isoproterenol concentration of 0.2 mg/mL.

10 mcg/mL = 0.01 mg/mL

0.01 mg/mL x 50 mL = 0.5 mg isoproterenol

$$\frac{0.5 \text{ mg}}{0.2 \text{ mg/mL}} = 2.5 \text{ mL of isoproterenol}$$

Add 2.5 mL of isoproterenol (0.2 mg/mL) to 47.5 mL of compatible solution (eg, D<sub>5</sub> W) to yield 50 mL of infusion solution with a concentration of 10 mcg/mL.

Maximum concentration 20 mcg/mL.

**Isoproterenol Titration Chart**

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
5	0.05	0.6
	0.1	1.2
	0.5	6
	1	12
10	0.05	0.3
	0.1	0.6
	0.5	3
	1	6
15	0.05	0.2
	0.1	0.4
	0.5	2
	1	4
20	0.05	0.15
	0.1	0.3
	0.5	1.5
	1	3

**Uses**

Increases cardiac output in patients with cardiovascular shock.  
Pulmonary vasodilator (older infants).

*continued...*

**Monitoring**

Continuous vital signs, intra-arterial blood pressure, CVP monitoring preferable. Periodic blood glucose reagent strips.

**Adverse Effects/Precautions**

Cardiac arrhythmias. Tachycardia severe enough to cause CHF. Decreases venous return to heart. Systemic vasodilation. May cause hypoxemia by increasing intrapulmonary shunt. Hypoglycemia.

**Pharmacology**

$\beta$ -receptor stimulant, sympathomimetic. Increases cardiac output by 1) increasing rate (major) and 2) increasing strength of contractions (minor). Insulin secretion is stimulated. Afterload reduction via  $\beta_2$  effects on arterioles.

**Special Considerations/Preparation**

Supplied as 0.2-mg/mL (1:5000) solution in 1-mL and 5-mL ampuls.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Amiodarone, caffeine citrate, calcium chloride, calcium gluceptate, cimetidine, dobutamine, famotidine, heparin, hydrocortisone succinate, milrinone, netilmicin, nitroprusside, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanyl, and vecuronium.

**Incompatibility:** Furosemide and sodium bicarbonate.

**Selected References**

- ◆ Cabal LA, Devaskar U, Siassi B, et al: Cardiogenic shock associated with perinatal asphyxia in preterm infants. *J Pediatr* 1980;96:705.
- ◆ Daoud FS, Reeves JT, Kelly DB: Isoproterenol as a potential pulmonary vasodilator in primary pulmonary hypertension. *Am J Cardiol* 1978;42:817.
- ◆ Product Information, Hospira, 2006

Compatibilities updated 7/2009

Text updated 3/2008

**Dose & Administration**

**Initial bolus dose:** 0.5 to 1 mg/kg IV push over 5 minutes. Repeat every 10 minutes as necessary to control arrhythmia. Maximum total bolus dose should not exceed 5 mg/kg.

**Maintenance IV infusion:** 10 to 50 mcg/kg per minute. Premature neonates should receive lowest dosage.

**Solution Preparation Calculations**

To calculate the **AMOUNT** of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the **VOLUME** of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

**Example (for Lidocaine):** Mix 50 mL of 2400 mcg/mL solution using lidocaine concentration of 20 mg/mL.

2400 mcg/mL = 2.4 mg/mL

2.4 mg/mL x 50 mL = 120 mg lidocaine

$$\frac{\text{*120 mg}}{\text{20 mg/mL}} = \text{6 mL of lidocaine}$$

Add 6 mL of lidocaine (20 mg/mL) to 44 mL of compatible solution (eg, D<sub>5</sub> W) to yield 50 mL of infusion solution with a concentration of 2400 mcg/mL.

Maximum concentration is 8000 mcg/mL.

*continued...*

Lidocaine Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
800	10	0.75
	20	1.5
	30	2.25
	40	3
	50	3.75
1600	10	0.375
	20	0.75
	30	1.125
	40	1.5
	50	1.875
2400	10	0.25
	20	0.5
	30	0.75
	40	1
	50	1.25
4000	10	0.15
	20	0.3
	30	0.45
	40	0.6
	50	0.75
6000	10	0.1
	20	0.2
	30	0.3
	40	0.4
	50	0.5
8000	10	0.075
	20	0.15
	30	0.225
	40	0.3
	50	0.375

**Uses**

Short-term control of ventricular arrhythmias, including ventricular tachycardia, premature ventricular contractions, and arrhythmias resulting from digitalis intoxication.

**Monitoring**

Continuous monitoring of EKG, heart rate, and blood pressure. Assess level of consciousness. Observe for seizure activity. Therapeutic total lidocaine serum concentrations are 1 to 5 mcg/mL.

**Adverse Effects/Precautions**

Early signs of CNS toxicity are drowsiness, agitation, vomiting, and muscle twitching. Later signs include seizures, loss of consciousness, respiratory depression, and apnea. Cardiac toxicity is associated with excessive doses and includes bradycardia, hypotension, heart block, and cardiovascular collapse.

**Contraindicated in infants with cardiac failure and heart block.** Serum lidocaine concentrations increase when using either cimetidine or propranolol in combination.

*continued...*

**Pharmacology**

Lidocaine is a Type 1b antiarrhythmic agent used intravenously. Onset of action is 1 to 2 minutes after bolus administration. Plasma half-life in neonates is 3 hours. Free drug fraction in both term and premature neonates is approximately twice that found in older children because of significantly reduced protein binding by  $\alpha_1$ -acid glycoprotein. Transformed in the liver to metabolites with antiarrhythmic activity; approximately 30% is excreted unchanged in neonates.

**Special Considerations/Preparation**

**Use only preservative-free lidocaine without epinephrine.** Available in multiple concentrations ranging from 1% to 20%. To make a dilution for bolus dosing, dilute 10 mg lidocaine (0.5 mL of 2% solution) in 9.5 mL NS or D<sub>5</sub>W, yielding a 1 mg/mL final concentration.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Alteplase, aminophylline, amiodarone, ampicillin, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefoxitin, chloramphenicol, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, flumazenil, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, insulin, linezolid, methicillin, metoclopramide, micafungin, morphine, nafcillin, nicardipine, nitroglycerin, penicillin G, pentobarbital, potassium chloride, procainamide, ranitidine, sodium bicarbonate, and sodium nitroprusside.

**Incompatibility:** Phenytoin.

**Selected References**

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- ◆ Gelband H, Rosen MR: Pharmacologic basis for the treatment of cardiac arrhythmias. *Pediatrics* 1975;55:59.

Compatibilities updated 7/2009

Text updated 3/2008



**Dose & Administration**

**Loading dose:** 75 mcg/kg IV infused over 60 minutes, immediately followed by

**Maintenance infusion:** 0.5 to 0.75 mcg/kg per minute.

Note: Above doses are from studies of older infants and children. Adjust infusion rate based upon hemodynamic and clinical response.

**Premature infants less than 30 weeks GA:**

**Loading dose:** 135 mcg/kg IV infused over 3 hours, immediately followed by

**Maintenance infusion:** 0.2 mcg/kg per minute.

(Preliminary data from pilot study referenced below)

**Uses**

Short term (less than 72 hours) treatment of acute low cardiac output after cardiac surgery or due to septic shock.

**Monitoring**

Continuous monitoring of blood pressure, heart rate and rhythm. Assess signs of cardiac output. Carefully monitor fluid and electrolyte changes and renal function during therapy. Monitor platelet counts.

**Adverse Effects/Precautions**

Assure adequate vascular volume prior to initiating therapy. Blood pressure will likely fall 5% to 9% after the loading dose, but should gradually return to baseline by 24 hours. Heart rate increases of 5% to 10% are also common. Thrombocytopenia was reported frequently in some studies and rarely in others. Arrhythmias occur occasionally.

**Pharmacology**

Milrinone improves cardiac output by enhancing myocardial contractility, enhancing myocardial diastolic relaxation and decreasing vascular resistance. It acts via selective phosphodiesterase III inhibition that leads to increased intracellular cyclic AMP, increased myocardial intracellular calcium, and increased reuptake of calcium after systole. Vasodilatation is related to increased levels of cyclic GMP in vascular smooth muscle. Unlike catecholamines, myocardial oxygen consumption is not increased. Elimination is primarily via renal mechanisms. Half-life is quite variable, ranging from approximately 10 hours in ELBW neonates to approximately 3 hours in older and more mature infants.

**Special Considerations/Preparation**

Available in 1-mg/mL solution for injection in 10-, 20-, and 50-mL single-dose vials. Dilute with compatible diluent prior to administration. **Maximum concentration for infusion is 200 mcg/mL.** Also available as premixed solution for injection (100-mL and 200-mL bags) in a concentration of 200 mcg/mL in 5% Dextrose (pH of 3.2 to 4).

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, NS, and LR.

**Terminal Injection Site Compatibility:** Dex/AA. Acyclovir, amikacin, aminophylline, amiodarone, ampicillin, atracurium, atropine, bumetanide, calcium chloride, calcium gluconate, cefazolin, cefepime, cefotaxime, ceftazidime, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, epinephrine, fentanyl, gentamicin, heparin, insulin, isoproterenol, lorazepam, meropenem, methylprednisolone, metronidazole, micafungin, midazolam, morphine, nicardipine, nitroglycerin, norepinephrine, oxacillin, pancuronium, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, propranolol, ranitidine, sodium bicarbonate, sodium nitroprusside, theophylline, ticarcillin, ticarcillin-clavulanate, tobramycin, vancomycin, and vecuronium.

**Incompatibility:** Furosemide, imipenem/cilastatin and procainamide.

### Selected References

- ◆ Paradisis M, Jiang X, McLachlan AJ, et al: Population pharmacokinetics and dosing regimen of milrinone in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F204-209.
- ◆ Hoffman TM, Wernovsky G, Atz AM, et al: Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. *Circulation* 2003;107:996-1002.
- ◆ Lindsay CA, Barton P, Lawless S, et al: Pharmacokinetics and pharmacodynamics of milrinone in pediatric patients with septic shock. *J Pediatr* 1998;132:329-34.
- ◆ Chang AC, Atz AM, Wernovsky G, et al: Milrinone: Systemic and pulmonary hemodynamic effects in neonates after cardiac surgery. *Crit Care Med* 1995;23:1907-14.
- ◆ Veltri MA, Conner KG: Physical compatibility of milrinone lactate injection with intravenous drugs commonly used in the pediatric intensive care unit. *Am J Health-Syst Pharm* 2002;59: 452-54.
- ◆ Akkerman SR, Zhang H, Mullins RE, Yaughn K: Stability of milrinone lactate in the presence of 29 critical care drugs and 4 i.v. solutions. *Am J Health-Syst Pharm* 1999;56:63-68.
- ◆ Paradisis M, Evans N, Kluckow M, et al: Pilot study of milrinone for prevention of low systemic blood flow in very preterm infants. *J Pediatr* 2006;148:306-313.
- ◆ Product Information, APP, 2008.

Dosing, Special Considerations, and References updated 12/2010  
Compatibilities updated 3/2007



**Dose & Administration**

**Initial dose:** 0.5 mcg/kg per minute continuous IV infusion.

Titrate dose to response. Blood pressure will begin to decrease within minutes of starting the infusion, reaching half of its ultimate decrease in approximately 45 minutes. Blood pressure equilibrium will not be achieved for approximately 50 hours (adult data).

Maintenance doses are usually 0.5 to 2 mcg/kg per minute.

**Uses**

Treatment of acute severe hypertension.

**Monitoring**

Continuous monitoring of blood pressure, heart rate and rhythm during initiation of therapy, and frequently thereafter. Observe IV site for signs of irritation.

**Adverse Effects/Precautions**

No adverse effects have been reported in neonates (small numbers). Hypotension and tachycardia are dose-dependent in adults. Headache, nausea, and vomiting were the other common effects reported.

**Pharmacology**

Nicardipine is a dihydropyridine calcium channel blocker that significantly decreases systemic vascular resistance. Unlike other calcium channel blockers, it has limited effects on the myocardium. It is extensively metabolized by the liver, and is highly protein bound. Following infusion in adults, nicardipine plasma concentrations decline tri-exponentially, with a rapid early distribution phase (alpha half-life of 2.7 minutes), an intermediate phase (beta half-life of 44.8 minutes), and a slow terminal phase (gamma half-life of 14.4 hours) that can only be detected after long-term infusions. Experience in neonates is limited, and there are no reported pharmacokinetic data.

**Special Considerations/Preparation**

Available as 2.5-mg/mL solution for injection in 10-mL ampules. **Dilute prior to administration to a concentration of 0.1 mg/mL.** Dilution is stable at room temperature for 24 hours. Also available as premixed solution (0.1 mg/mL, 0.2 mg/mL; 200 mL) in dextrose or sodium chloride. Store ampuls and premixed solution at controlled room temperature in carton until ready to use. Freezing does not adversely affect the product, but exposure to elevated temperatures should be avoided. Protect from light.

**Solution Compatibility:** D<sub>5</sub>W, NS, and D<sub>5</sub>NS.

**Solution Incompatibility:** Lactated Ringer's.

*continued...*

**Terminal Injection Site Compatibility:** No data available for Dex/AA solutions or fat emulsions.

Amikacin, aminophylline, aztreonam, calcium gluconate, cefazolin, ceftizoxime, chloramphenicol, cimetidine, clindamycin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, gentamicin, heparin (concentrations less than or equal to 1 unit/mL), hydrocortisone, lidocaine, linezolid, lorazepam, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, nafcillin, nitroglycerin, norepinephrine, penicillin G potassium, piperacillin, potassium chloride, potassium phosphate, ranitidine, sodium acetate, sodium nitroprusside, tobramycin, trimethoprim/sulfamethoxazole, vancomycin, and vecuronium.

**Incompatibility:** Ampicillin, cefepime, cefoperazone, ceftazidime, furosemide, heparin (concentrations greater than 1 unit/mL), miconazole, sodium bicarbonate and thiopental.

### Selected References

- ◆ McBride BF, White CM, Campbell M, Frey BM: Nicardipine to control neonatal hypertension during extracorporeal membrane oxygen support. *Ann Pharmacother* 2003;37:667-670.
- ◆ Tobias JD: Nicardipine to control mean arterial pressure after cardiothoracic surgery in infants and children. *Am J Ther* 2001;8:3-6.
- ◆ Milou C, Debuche-Benouachkou V, Semama DS et al: Intravenous nicardipine as a first-line antihypertensive drug in neonates. *Intensive Care Med* 2000;26:956-958.
- ◆ Gouyon JB, Geneste B, Semama DS, et al: Intravenous nicardipine in hypertensive preterm infants. *Arch Dis Child Fetal Neonatal Ed* 1997;76:F126-127.
- ◆ Product Information, Baxter 2009.
- ◆ Product Information, Teva, 2008.

Special Considerations and References updated 12/2010

Compatibilities updated 7/2009

Added 3/2005

**Dose & Administration**

30 mg per 250 mL of arterial catheter infusion solution.

**Uses**

Prolongation of peripheral arterial catheter patency.

**Adverse Effects/Precautions**

Use with caution in VLBW infants in the first days after birth due to potential of developing or extending an intracranial hemorrhage. Chronic hepatitis, as evidenced by an increase in serum bilirubin and serum glutamic transaminase, has been reported in three adults following long-term papaverine therapy. One patient had jaundice, and another had abnormal liver function on biopsy.

**Pharmacology**

Papaverine directly relaxes the tonus of various smooth muscle, especially when it has been spasmodically contracted. It relaxes the smooth musculature of the larger blood vessels, especially coronary, systemic peripheral and pulmonary arteries. Vasodilation may be related to its ability to inhibit cyclic nucleotide phosphodiesterase, thus increasing levels of intracellular cyclic AMP. During administration, the muscle cell is not paralyzed and still responds to drugs and other stimuli causing contraction. Possibly because of its direct vasodilating action on cerebral blood vessels, papaverine increases cerebral blood flow and decreases cerebral vascular resistance in healthy subjects; oxygen consumption is unaltered. Papaverine is metabolized in the liver and excreted in the urine in an inactive form.

**Special Considerations/Preparation**

Supplied as 30 mg/mL solution for injection in 2 mL preservative-free vials and 10-mL multiple dose vials containing 0.5% chlorobutanol.

**Solution Compatibility:** NS, 0.45 NS, both with 1 unit/mL heparin.

**Solution Incompatibility:** Lactated Ringer's (precipitate forms).

**Terminal Injection Site Compatibility:** Phentolamine.

**Selected References**

- ◆ Griffin MP, Siadat MS: Papaverine prolongs patency of peripheral arterial catheters in neonates. *J Pediatr* 2005;146:62-65.
- ◆ Heullitt MJ, Farrington EA, O'Shea TM, et al: Double-blind randomized controlled trial of papaverine-containing solutions to prevent failure of arterial catheters in pediatric patients. *Crit Care Med* 1993;21:825-829.
- ◆ Product Information, Parenta Pharmaceuticals, Inc., 2006.

Added 3/2005

**Dose & Administration**

Inject a 0.5-mg/mL solution of phentolamine subcutaneously into the affected area. Usual amount needed is 1 to 5 mL, depending on the size of the infiltrate. May be repeated if necessary.

**Uses**

Prevention of dermal necrosis and sloughing caused by extravasation of vasoconstrictive agents, eg, dopamine.

**Monitoring**

Assess affected area for reversal of ischemia. Monitor blood pressure.

**Adverse Effects/Precautions**

Hypotension could potentially occur if a very large dose is administered. Consider using topical 2% nitroglycerin ointment if affected extremity is significantly swollen.

**Pharmacology**

Alpha-adrenergic blocking agent that produces peripheral vasodilation, thereby reversing ischemia produced by vasopressor infiltration. The effect should be seen almost immediately. Biological half-life when injected subcutaneously is less than 20 minutes.

**Special Considerations/Preparation**

Available in 5-mg vial as a lyophilized powder.

To prepare:

- 1) Reconstitute one vial with 1 mL of normal saline.
- 2) Dilute to a concentration of 0.5 mg/mL with 9 mL normal saline. Use immediately. **Do not use if solution is discolored or contains particulate contamination.**

**Terminal Injection Site Compatibility:** Amiodarone, dobutamine, and papaverine.

**Selected References**

- ♦ Subhani M, Sridhar S, DeCristofaro JD: Phentolamine use in a neonate for the prevention of dermal necrosis caused by dopamine: A case report. *J Perinatol* 2001;21:324-326.
- ♦ Denkler KA, Cohen BE: Reversal of dopamine extravasation injury with topical nitroglycerin ointment. *Plast Reconstr Surg* 1989;84:811.
- ♦ Siwy BK, Sadove AM: Acute management of dopamine infiltration injury with Regitine. *Plast Reconstr Surg* 1987;80:610.
- ♦ Product Information, Bedford, 1999

Dose & Administration and Special Considerations updated 3/3009

Compatibilities updated 3/2005

**Dose & Administration**

**Initial bolus dose:** 7 to 10 mg/kg IV over 1 hour via syringe pump.

**Maintenance IV infusion:** 20 to 80 mcg/kg per minute. Premature neonates should receive the lowest dose.

**Uses**

Acute treatment of supraventricular tachycardia (SVT) refractory to vagal maneuvers and adenosine. Acute treatment of ventricular tachycardia unresponsive to cardioversion and adenosine. Ectopic tachycardia, junctional ectopic tachycardia, and atrial flutter. Consider obtaining expert consultation before use.

**Monitoring**

Continuous monitoring of the EKG, blood pressure and heart rate. Measure procainamide and N-acetyl procainamide (NAPA) concentrations at 2, 12, and 24 hours after starting the loading dose infusion.

**Therapeutic concentrations:**

Procainamide: 4 to 10 mcg/mL, NAPA 6 to 20 mcg/mL.

Sum of procainamide and NAPA: 10 to 30 mcg/mL.

**Adverse Effects/Precautions**

Severe hypotension with rapid infusion, bradycardia, A-V block, and ventricular fibrillation have been reported in adult patients. Normal procainamide concentrations widen the QRS complex due to slowing of conduction in the Purkinje system and ventricular muscle. The drug should be discontinued if the QRS duration increases by more than 35 to 50 percent to avoid serious toxicity. Adverse effects are reversible with discontinuation of drug.

**Black Box Warning**

According to the manufacturer's black box warning, agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia, and thrombocytopenia, some of which were fatal, have been reported (in adults).

**Pharmacology**

Procainamide is a class IA antiarrhythmic agent that increases the effective refractory period of the atria and the ventricles of the heart. Onset of action occurs within minutes of starting the loading dose. Half-life is approximately 5 hours in the term neonate, and longer in preterms. Metabolized primarily (60%) in the liver to N-acetylprocainamide (NAPA), an active metabolite. The rate of acetylation is primarily genetically determined in adults and children. Preterm neonates have a higher NAPA:procainamide ratio than term infants presumably due to delayed excretion of NAPA. Renal function is a significant determinant of procainamide clearance. Cimetidine and amiodarone interact when given with procainamide, increasing procainamide serum levels.

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**Special Considerations/Preparation**

Available in 10-mL vials providing 100 mg/mL or 2-mL vials providing 500 mg/mL. Store at room temperature. **DO NOT FREEZE.**

Dilute initial bolus dose to a final concentration of 20 mg/mL and administer over 1 hour. Maintenance infusion should be diluted to 2 mg/mL before administration.

**Solution Compatibility:** 0.45% NaCl and NS.

**Solution Incompatibility:** D<sub>5</sub>W.

**Terminal Injection Site Compatibility:** Amiodarone, dobutamine, famotidine, flumazenil, heparin, hydrocortisone, lidocaine, netilmicin, ranitidine, remifentanyl, and sodium nitroprusside.

**Incompatibility:** Esmolol, milrinone, and phenytoin.

**Selected References**

- ◆ Moffett BS, Cannon BC, Friedman RA, Kertesz NJ: Therapeutic levels of intravenous procainamide in neonates: A retrospective assessment. *Pharmacotherapy* 2006;26:1687-1693.
- ◆ Wong KK, Potts JE, Ethridge SP, Sanatani S: Medications used to manage supraventricular tachycardia in the infant: a North American survey. *Pediatr Cardiol* 2006;27:199-203.
- ◆ Sianipar A, Parkin JE and Sunderland B: Chemical incompatibility between procainamide hydrochloride and glucose following intravenous admixture. *J Pharm Pharmacol* 1994;46:951-955.
- ◆ Bryson SM, Leson CL, Irwin DB, et al: Therapeutic monitoring and pharmacokinetic evaluation of procainamide in neonates. *DISP* 1991;25:68-71.
- ◆ Raymond GG, Reed MT, Teagarden JR, et al: Stability of procainamide hydrochloride in neutralized 5% dextrose injection. *Am J Hosp Pharm* 1988;45:2513-2517.
- ◆ Product Information, Hospira, 2004

Compatibilities and References updated 7/2009

Adverse Effects/Precautions updated 1/2009

Added 3/2007

**Dose & Administration****Hypertension and Tachyarrhythmias**

**Starting oral dose:** 0.25 mg/kg per dose every 6 hours.

Increase as needed to maximum of 3.5 mg/kg per dose every 6 hours.

**Starting IV dose:** 0.01 mg/kg every 6 hours over 10 minutes.

Increase as needed to maximum of 0.15 mg/kg per dose every 6 hours. Effective dosage requirements will vary significantly.

**Infantile Hemangiomas**

Usual maintenance doses have been 2 to 3 mg/kg/day orally in 3 divided doses. Initial doses of 2 mg/kg/day orally in 3 divided doses have been used while some authors recommend starting at 0.3 to 1 mg/kg/day to assess tolerability and then increasing to 2 mg/kg/day incrementally over several days. Tapering periods have ranged from 2 weeks to 1 month.

For infants receiving propranolol, regular, frequent food intake (every 3 to 4 hours) is an important consideration with regards to risks for hypoglycemia.

**Uses**

Treatment of tachyarrhythmias and hypertension. Preferred therapy for SVT if associated with Wolff-Parkinson-White syndrome. Palliation of tetralogy of Fallot and hypertrophic obstructive cardiomyopathy. Adjunctive treatment of neonatal thyrotoxicosis. Treatment of infantile hemangiomas.

**Monitoring**

Continuous ECG monitoring should be done during acute treatment of arrhythmias and during IV therapy. Measure systemic blood pressure frequently. Monitor vital signs and measure blood glucose during initiation of treatment and after dosage changes. Assess for increased airway resistance.

**Adverse Effects/Precautions**

Contraindicated in patients with cardiogenic shock, sinus bradycardia greater than first degree block, reactive airway disease, or diminished myocardial contractility. Adverse effects are related to beta-receptor blockade: Bradycardia, bronchospasm, and hypoglycemia are most frequently reported. Hypotension occurs in patients with underlying myocardial dysfunction. A withdrawal syndrome (nervousness, tachycardia, sweating, hypertension) has been associated with sudden cessation of the drug. Asymptomatic and symptomatic hypoglycemia, requiring hospitalization, have been reported in infants receiving propranolol for the treatment of infantile hemangioma. Infants less than 3 months of age are at increased risk.

**Pharmacology**

Propranolol is the most widely used nonselective  $\beta$ -adrenergic-receptor blocking agent. Peak serum concentration is reached approximately 2 hours after an oral dose. Propranolol undergoes significant first-pass hepatic metabolism, resulting in 30% to 40% bioavailability. Protein binding is 70% in neonates. Serum half-life is prolonged in patients with liver disease. Elimination is by renal excretion of metabolites.

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### Special Considerations/Preparation

Oral solution is available in concentrations of 4 mg/mL and 8 mg/mL (contains 0.6% alcohol). Injectable form is available in 1-mL vials containing 1 mg.

Make a 0.1 mg/mL dilution by adding 1 vial to 9 mL preservative-free normal saline. **Protect from light.** Store at room temperature.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Alteplase, dobutamine, heparin, hydrocortisone succinate, linezolid, milrinone, morphine, potassium chloride, and propofol.

### Selected References

- ◆ Buckmiller LM, Munson PD, Dyamenahalli U, et al: Propranolol for infantile hemangiomas: Early experience at a tertiary vascular anomalies center. *Laryngoscope* 2010;120:676-681.
- ◆ Holland KE, Frieden IJ, Frommelt PC, et al: Hypoglycemia in children taking propranolol for the treatment of infantile hemangioma. *Arch Dermatol* 2010;146:775-778.
- ◆ Mazereeuw-Hautier J, Hoeger PH, Benlahrech S, et al: Efficacy of propranolol in hepatic infantile hemangiomas with diffuse neonatal hemangiomatosis. *J Pediatr* 2010;157:340-342.
- ◆ Schiestl C, Neuhaus K, Zoller S, et al: Efficacy and safety of propranolol as first-line treatment for infantile hemangiomas. *Eur J Pediatr* 2010;Oct 9 [Epub ahead of print].
- ◆ Vanlander A, Decaluwe W, Vandelanotte M, et al: Propranolol as a novel treatment for congenital visceral haemangioma. *Neonatology* 2010;98:229-231.
- ◆ Lawley LP, Siegfried E, Todd JL: Propranolol treatment for hemangioma of infancy: risks and recommendations. *Pediatr Dermatol* 2009;26:610-614.
- ◆ Sans V, de la Roque ED, Berge J, et al: Propranolol for severe infantile hemangiomas: Follow-up report. *Pediatrics* 2009;124:e423-e431.
- ◆ Schneeweiss A: Neonatal cardiovascular pharmacology, in Long WA (ed): *Fetal and Neonatal Cardiology*. Baltimore: WB Saunders Co, 1990, p 675.
- ◆ Pickoff AS, Zies L, Ferrer PL, et al: High-dose propranolol therapy in the management of supraventricular tachycardia. *J Pediatr* 1979;94:144.
- ◆ Gillette P, Garson A, Eterovic E, et al: Oral propranolol treatment in infants and children. *J Pediatr* 1978;92:141.
- ◆ Product Information, Roxane, 2007.

Dose & Administration, Uses, Adverse Effects/Precautions and References updated 12/2010.



**Dose & Administration**

Time since last heparin dose in minutes and protamine dose:

Less than 30 min: 1 mg per 100 units heparin received.

30 to 60 min: 0.5 to 0.75 mg per 100 units heparin received.

60 to 120 min: 0.375 to 0.5 mg per 100 units heparin received.

Greater than 120 min: 0.25 to 0.375 mg per 100 units heparin received.

Maximum dose: 50 mg

Infusion rate: should not exceed 5 mg/min

**Uses**

Heparin antagonist.

**Monitoring**

Monitor vital signs, clotting functions, and blood pressure continuously. Observe for bleeding.

**Adverse Effects/Precautions****Black Box Warning**

Hypotension, cardiovascular collapse, pulmonary edema, pulmonary vasoconstriction, and pulmonary hypertension may occur. Risk factors for severe protamine adverse reactions include high doses, rapid administration, repeated doses, previous exposure to protamine or protamine-containing drugs (eg, NPH insulin, protamine zinc insulin, and certain beta blockers), severe left ventricular dysfunction, and abnormal preoperative pulmonary hemodynamics. Vasopressors and resuscitation equipment should be available. Should not be used for bleeding occurring without prior heparin use.

Excessive doses can cause serious bleeding problems. Hypotension, bradycardia, dyspnea, and transitory flushing have been reported in adults.

**Pharmacology**

Anticoagulant when given alone. Combines ionically with heparin to form a stable complex devoid of anticoagulant activity. Rapid action after IV use (5 minutes).

**Special Considerations/Preparation**

Available as a 10-mg/mL concentration preservative-free in 5- and 25-mL vials. Store at room temperature. Can be diluted in D<sub>5</sub>W or NS.

**Solution Compatibility:** D<sub>5</sub>W and NS. No data are currently available on Dex/AA.

**Terminal Injection Site Compatibility:** Cimetidine and ranitidine.

**Incompatibility:** Most cephalosporins and penicillins.

**Selected References**

◆ Monagle P, Chalmers E, Chan A, et al: Antithrombotic therapy in neonates and children: Antithrombotic and thrombolytic therapy, 8th Ed. *Chest* 2008;133:887S-968S.

◆ Product Information, APP, 2008.

Adverse Effects/Precautions and References updated 12/2010

Compatibilities updated 7/2009



**Dose & Administration**

**IV:** Administer a loading dose of 0.4 mg/kg over 3 hours, followed by a continuous infusion of 1.6 mg/kg per day (0.067 mg/kg per hour).

**Oral:** 0.5 to 2 mg/kg per dose every 6 to 12 hours.

Some authors have successfully used doses of 3 mg/kg per dose orally every 6 hours.

Pharmacokinetics of sildenafil in neonates are highly variable. Careful dose titration while monitoring oxygenation and blood pressure is required.

**Uses**

Limited to treatment of patients with persistent pulmonary hypertension refractory to inhaled nitric oxide and other conventional therapies, those who are persistently unable to be weaned off of inhaled nitric oxide, or in situations where nitric oxide is not available. It has also been reported to improve pulmonary blood flow in patients with severe Ebstein's anomaly.

**Monitoring**

Continuous monitoring of blood pressure and oxygenation.

**Adverse Effects/Precautions**

Use in neonates should be restricted and considered experimental. Data in neonates remain limited. The most concerning short term adverse effects are worsening oxygenation and systemic hypotension. There is one case report of bleeding after circumcision in a neonate receiving chronic therapy. Use with caution in infants with sepsis. Sildenafil causes transient impairment of color discrimination in adults, and there is concern that it could increase the risk of severe retinopathy of prematurity if used in extremely premature infants.

**Pharmacology**

Sildenafil is a selective phosphodiesterase (PDE5) inhibitor. This inhibition leads to accumulation of cyclic GMP in pulmonary smooth muscle cells, causing pulmonary vascular relaxation. It may also potentiate the effect of inhaled nitric oxide. Pharmacokinetics in neonates receiving sildenafil, both intravenously and orally, are highly variable. Oral absorption is rapid in adults with approximately 40% bioavailability; peak concentrations are reached in 30 to 120 minutes. Protein binding is 94%. It is metabolized primarily by hepatic CYP3A4 to an active metabolite (N-desmethyl sildenafil) that also has PDE5 inhibitory activity. The terminal half-life of sildenafil in neonates on Day 1 of life is estimated to be 56 hours, and that of the metabolite 10 hours. This compares to adult data where both sildenafil and the metabolite have terminal half-lives of 4 hours. Clearance increases rapidly (triples) in the first week of life, likely related to both maturation and improvements in patient hemodynamics. Patients with significant hepatic or renal dysfunction have reduced clearance. Significant increases in sildenafil concentrations may occur when used concomitantly with drugs that are CYP3A4 inhibitors: eg, fluconazole, erythromycin, amiloridine, and cimetidine.

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### Special Considerations/Preparation

Revatio® is supplied as 20-mg tablets and as a single-use vial containing 10 mg (12.5 mL) of sildenafil, equivalent to 0.8 mg sildenafil per mL. Each mL of solution also contains 50.5 mg dextrose and water for injection. Viagra® is supplied as 25-mg, 50-mg, and 100-mg tablets.

To prepare an oral 2.5-mg/mL suspension (150 mL), thoroughly crush fifteen 25-mg tablets into a fine powder and add a 1:1 mixture of Ora-Sweet® and Ora-Plus® or methylcellulose 1% and Simple Syrup, NF to make a final concentration of 2.5 mg/mL. Suspension is stable for 91 days in plastic bottles at 4 and 25 degrees C. This extemporaneous suspension was made using the Viagra® (sildenafil) dosage form.

### Selected References

- ◆ Steinhorn RH, Kinsella JP, Pierce C, et al: Intravenous sildenafil in the treatment of neonates with persistent pulmonary hypertension. *J Pediatr* 2009;155:841-847.
- ◆ Ahsman MJ, Witjes BCM, Wilschut ED, et al: Sildenafil exposure in neonates with pulmonary hypertension after administration via a nasogastric tube. *Arch Dis Child Fetal Neonatal Ed* 2009; Nov 30 [Epub ahead of print].
- ◆ Mukherjee A, Dombi T, Wittke B, Lalonde R: Population pharmacokinetics of sildenafil in term neonates: evidence of rapid maturation of metabolic clearance in the early postnatal period. *Clin Pharmacol Ther* 2009;85:56-63.
- ◆ Vargas-Origel A, Gomez-Rodriguez G, Aldana-Valenzuela C, et al: The use of sildenafil in persistent pulmonary hypertension of the newborn. *Am J Perinatol* 2009; Oct 28 [Epub ahead of print].
- ◆ Gamboa D, Robbins D, Saba Z: Bleeding after circumcision in a newborn receiving sildenafil. *Clin Pediatr* 2007;46:842-43.
- ◆ Noori S, Friedlich P, Wong P, et al: Cardiovascular effects of sildenafil in neonates and infants with congenital diaphragmatic hernia and pulmonary hypertension. *Neonatology* 2007;91:92-100.
- ◆ Baquero H, Soliz A, Neira F, et al: Oral sildenafil in infants with persistent pulmonary hypertension of the newborn: a pilot randomized blinded study. *Pediatrics* 2006;117:1077-1083.
- ◆ Nahata MC, Morosco RS, Brady MT: Extemporaneous sildenafil citrate oral suspensions for the treatment of pulmonary hypertension in children. *Am J Health-Syst Pharm* 2006;63:254-257.
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- ◆ Travadi JN, Patole SK: Phosphodiesterase inhibitors for persistent pulmonary hypertension of the newborn: a review. *Pediatr Pulmonol* 2003;36:529-535.
- ◆ Atz AM, Wessel DL: Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. *Anesthesiology* 1999;91:307-310.
- ◆ Product Information, Pfizer, 2010

Special Considerations and References updated 12/2010.  
Dose & Administration and Pharmacology updated 1/2010.  
Uses updated 3/2008.  
Added 3/2006

**Dose & Administration**

**Initial Dose:** 0.25 to 0.5 mcg/kg per minute continuous IV infusion by syringe pump. Use a large vein for IV.

Titrate dose upward every 20 minutes until desired response is attained.

Usual **maintenance dose** is less than 2 mcg/kg per minute.

For hypertensive crisis, may use up to 10 mcg/kg per minute, but for no longer than 10 minutes.

Sodium thiosulfate has been coadministered with sodium nitroprusside to accelerate the metabolism of cyanide; however, this has not been extensively studied.

**Uses**

Acute treatment of hypertensive emergencies. Acute afterload reduction in patients with refractory congestive heart failure.

**Monitoring**

Continuous heart rate and intra-arterial blood pressure monitoring is mandatory. Daily measurement of RBC cyanide (should be less than 200 ng/mL) and serum thiocyanate (should be less than 50 mcg/mL) concentrations. Assess frequently for development of metabolic acidosis. Daily assessment of renal and hepatic function. Monitor IV site closely.

**Adverse Effects/Precautions**

Severe hypotension and tachycardia. Cyanide toxicity may occur with prolonged treatment (greater than 3 days) and high (greater than 3 mcg/kg per minute) doses. Use with caution in liver and renal failure patients due to possible impairment of the metabolism of cyanide to thiocyanate. Extravasation can cause tissue sloughing and necrosis.

**Black Box Warning**

According to the manufacturer's black box warning, nitroprusside is not suitable for direct injection; the reconstituted solution must be further diluted in sterile 5% dextrose injection before infusion. Monitor acid-base balance and venous oxygen concentration while on therapy as these tests may indicate cyanide toxicity.

**Pharmacology**

Direct-acting nonselective (arterial and venous) vasodilator. Immediately interacts with RBC oxyhemoglobin, dissociating and forming methemoglobin with release of cyanide and nitric oxide. Rapid onset of action with a serum half-life of 3 to 4 minutes in adults. Further metabolized to thiocyanate in the liver and kidney. Thiocyanate is renally eliminated with a half-life of 4 to 7 days.

*continued...*

**Special Considerations/Preparation**

Available as powder for injection in 2 mL single-dose 50 mg vials. Reconstitute contents of vial with 2 to 3 mL of D<sub>5</sub>W or NS.

**Do not administer reconstituted drug directly from vial.** Dilute entire vial contents to a final concentration less than or equal to 200 mcg/mL (0.2 mg/mL) in D<sub>5</sub>W or NS. Use within 24 hours of preparation.

**Protect from light** with aluminum foil or other opaque material. Blue, green or deep red discoloration indicates nitroprusside inactivation. Slight brownish discoloration is common and not significant.

**Solution Compatibility:** D<sub>5</sub>W, NS, and LR only.

**Terminal Injection Site Compatibility:** Caffeine citrate, calcium chloride, cimetidine, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, famotidine, furosemide, heparin, indomethacin, insulin, isoproterenol, lidocaine, magnesium, miconazole, midazolam, milrinone, morphine, nicardipine, nitroglycerin, pancuronium, potassium chloride, procainamide, propofol, prostaglandin E<sub>1</sub>, ranitidine, and vecuronium.

**Incompatibility:** Amiodarone.

**Selected References**

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Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

Text updated 3/2008

Added 3/1996

**Dose & Administration**

**Initial dose:** 1 mg/kg per dose orally every 12 hours.

Gradually increase as needed every 3 to 5 days until stable rhythm is maintained.

**Maximum dose:** 4 mg/kg per dose orally every 12 hours.

**Uses**

Treatment of refractory ventricular and supraventricular tachyarrhythmias.

**Monitoring**

Frequent EKG during initiation of therapy.

**Adverse Effects/Precautions**

Proarrhythmic effects occur in 10% of pediatric patients: sinoatrial block, A-V block, torsades de pointes and ventricular ectopic activity. These effects usually occur in the first few days of treatment. Prolongation of the QT interval is dose-dependent. Other adverse effects include fatigue, dyspnea, and hypotension.

**Black Box Warning**

According to the manufacturer's black box warning, to minimize the risk of induced arrhythmia, patients initiated or re-initiated on sotalol should receive continuous cardiac monitoring for a minimum of three days on maintenance doses.

**Pharmacology**

Sotalol is an antiarrhythmic agent that combines Class II beta-blocking properties with Class III prolongation of cardiac action potential duration. Betapace® is a racemic mixture of *d*- and *l*-sotalol. Oral bioavailability is good, but absorption is decreased by 20% to 30% by food, especially milk. Sotalol does not bind to plasma proteins, is not metabolized, and is renally excreted as unchanged drug. Limited pharmacokinetic data in infants show a half-life of 8 hours, increasing significantly in elderly patients and those with renal dysfunction.

**Special Considerations/Preparation**

Oral formulation supplied in 80-mg, 120-mg, 160-mg, and 240-mg tablets.

A 5 mg/mL oral suspension may be made as follows: crush 5 (five) 120-mg tablets and add to 120 mL of OraPlus®:OraSweet® (1:1) or 1% methylcellulose:Simple Syrup NF (1:9) in a 6-ounce amber plastic bottle. Shake to adequately suspend. Stable for 90 days at room temperature or refrigerated.

*continued...*

**Selected References**

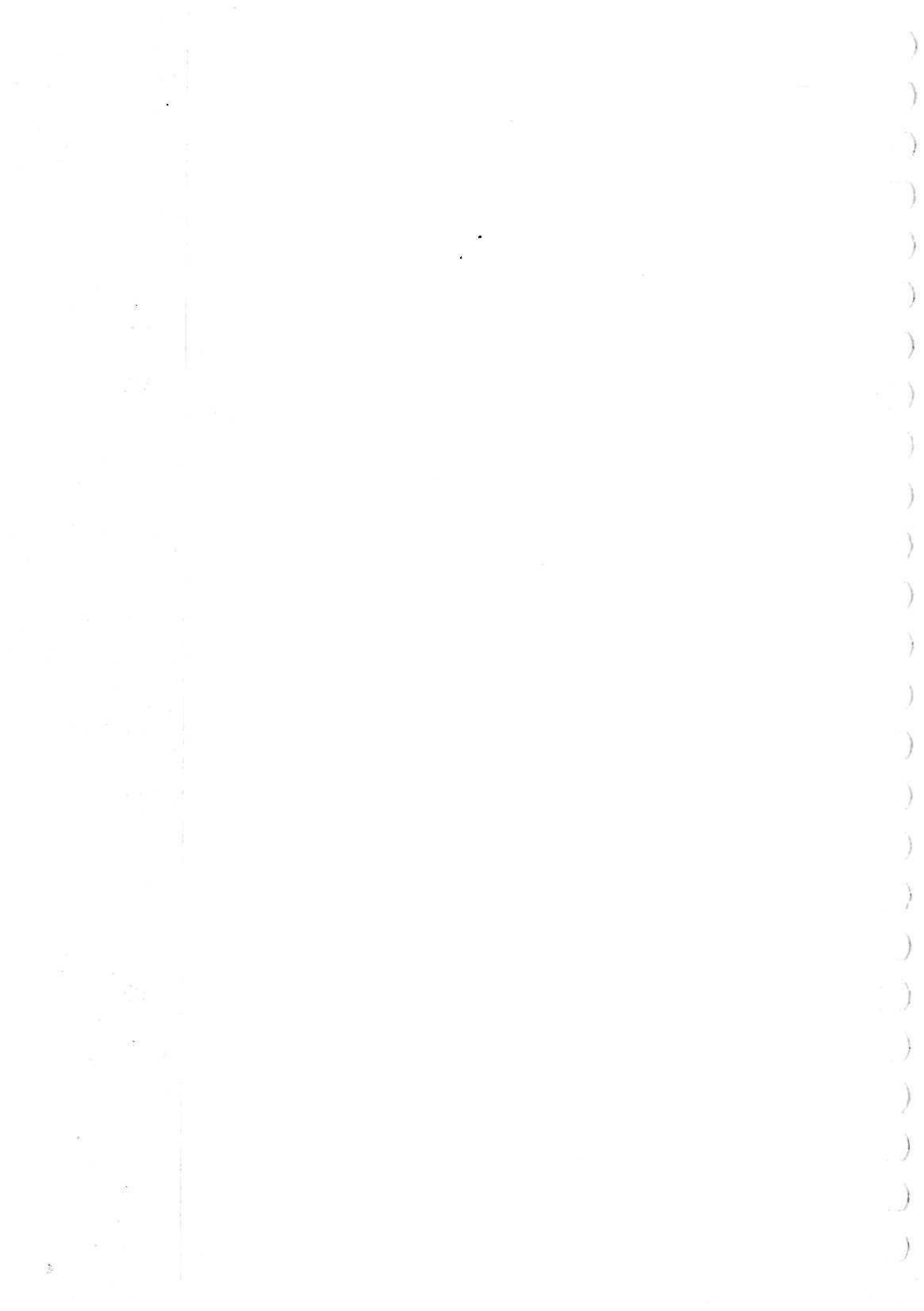
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Special Considerations and References updated 12/2010

Adverse Effects/Precautions updated 1/2009

Pharmacology updated 3/2001





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## CNS DRUGS

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**Dose & Administration**

**Oral Loading dose:** 20 to 25 mg/kg. Maintenance: 12 to 15 mg/kg per dose.

**Rectal Loading dose:** 30 mg/kg. Maintenance: 12 to 18 mg/kg per dose.

**Maintenance intervals:** Term infants: every 6 hours

Preterm infants greater than or equal to 32 weeks Postmenstrual Age: every 8 hours

Preterm infants less than 32 weeks Postmenstrual Age: every 12 hours

**Uses**

Fever reduction and treatment of mild to moderate pain.

Routine prophylactic use of acetaminophen at the time of vaccination is not recommended because of a potential reduction in antibody response.

**Monitoring**

Assess for signs of pain. Monitor temperature. Assess liver function.

Serum acetaminophen concentration is obtained only to assess toxicity.

**Adverse Effects/Precautions**

Liver toxicity occurs with excessive doses or after prolonged administration (greater than 48 hours) of therapeutic doses. Rash, fever, thrombocytopenia, leukopenia, and neutropenia have been reported in children.

**Pharmacology**

Nonnarcotic analgesic and antipyretic. Peak serum concentration occurs approximately 60 minutes after an oral dose. Absorption after rectal administration is variable and prolonged. Extensively metabolized in the liver, primarily by sulfation with a small amount by glucuronidation. Metabolites and unchanged drug are excreted by the kidney. Elimination half-life is approximately 3 hours in term neonates, 5 hours in preterm neonates greater than 32 weeks gestation, and up to 11 hours in more immature neonates. Elimination is prolonged in patients with liver dysfunction.

**Special Considerations/Preparation**

**Dosage forms:** Drops: 100 mg/mL, 48 mg/mL (alcohol-free).

Elixir: 16 mg/mL, 24 mg/mL, 32 mg/mL.

Liquid: 32 mg/mL (alcohol-free). Liquid: 33.33 mg/mL (7% alcohol).

Suppositories: 80, 120, 325, and 650 mg.

Inaccurate dosing may occur with rectal administration because of unequal distribution of acetaminophen in the suppositories.

**Treatment of Serious Acetaminophen Toxicity:** N-acetylcysteine (NAC), 150 mg/kg in 5% dextrose or 1/2 NS given IV over 60 minutes (loading dose), followed by 50 mg/kg in 5% dextrose or 1/2 NS over 4 hours, then 100 mg/kg in 5% dextrose or 1/2 NS over 16 hours. NAC should be continued until clinical and biochemical markers of hepatic injury improve, and acetaminophen concentration is below the limits of detection. NAC solution concentrations of 40 mg/mL have been used to avoid fluid overload and hyponatremia in the neonate.

*continued...*

**Selected References**

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Uses and References updated 12/2010

**Dose & Administration**

25 to 75 mg/kg per dose orally or rectally. Oral preparation should be diluted or administered after a feeding to reduce gastric irritation.

**Uses**

Sedative/hypnotic for short-term use only. Chloral hydrate has no analgesic properties; excitement may occur in patients with pain.

**Monitoring**

Assess level of sedation.

**Adverse Effects/Precautions**

Episodes of bradycardia are more frequent for up to 24 hours after a single dose in former premature infants. Gastric irritation and paradoxical excitement may also occur after a single dose. Other toxic effects have generally been reported in patients who received either repeated doses at regular intervals or acute overdoses. These effects may persist for days and include CNS, respiratory, and myocardial depression; cardiac arrhythmias; and ileus and bladder atony. Indirect hyperbilirubinemia may occur because TCE and bilirubin compete for hepatic conjugation. **Do not use in patients with significant hepatic and/or renal disease.**

**Pharmacology**

Well absorbed from the oral route, with the onset of action in 10 to 15 minutes. Chloral hydrate is rapidly converted by alcohol dehydrogenase to the active and potentially toxic metabolite trichloroethanol (TCEt), which is excreted renally after glucuronidation in the liver. It is also metabolized to trichloroacetic acid (TCA), which is carcinogenic in mice when given in very high doses. Both TCEt (8 to 64 hours) and TCA (days) have long serum half-lives in neonates and accumulate with repeated doses.

**Special Considerations/Preparation**

Chloral hydrate is available in syrup as 100-mg/mL concentration. Osmolality is 3285 mOsm/kg of water. **The preparations are light-sensitive: Store in a dark container.** Also available as 500 mg suppository. Inaccurate dosing may occur with rectal administration because of unequal distribution of chloral hydrate in the suppositories.

**Selected References**

- ◆ Allegaert K, Daniels H, Naulaers G, et al: Pharmacodynamics of chloral hydrate in former premature infants. *Eur J Pediatr* 2005;164:403-407.
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Updated 3/2006



**Dose & Administration**

**Sedation and analgesia:** 0.5 to 4 mcg/kg per dose IV slow push.  
Repeat as required (usually every 2 to 4 hours).

**Infusion rate:** 1 to 5 mcg/kg per hour.

Tolerance may develop rapidly following constant infusion.

**Anesthesia:** 5 to 50 mcg/kg per dose.

**Uses**

Analgesia. Sedation. Anesthesia.

**Monitoring**

Monitor respiratory and cardiovascular status closely. Observe for abdominal distention, loss of bowel sounds, and muscle rigidity.

**Adverse Effects/Precautions**

Respiratory depression occurs when anesthetic doses (greater than 5 mcg/kg) are used and may also occur unexpectedly because of redistribution. Chest wall rigidity has occurred in 4% of neonates who received 2.2 to 6.5 mcg/kg per dose, occasionally associated with laryngospasm. This was reversible with administration of naloxone. Urinary retention may occur when using continuous infusions. Tolerance may develop to analgesic doses with prolonged use. Significant withdrawal symptoms have been reported in patients treated with continuous infusion for 5 days or longer.

**Pharmacology**

Synthetic opioid narcotic analgesic that is 50 to 100 times more potent than morphine on a weight basis. Extremely lipid soluble. Penetrates the CNS rapidly. Transient rebound in fentanyl serum concentration may reflect sequestration and subsequent release of fentanyl from body fat. Metabolized extensively in the liver by CYP 3A4 enzyme system and then excreted by the kidney. Serum half-life is prolonged in patients with liver failure. Highly protein bound. Wide variability in apparent volume of distribution (10 to 30 L/kg) and serum half-life (1 to 15 hours).

**Special Considerations/Preparation**

**Naloxone should be readily available to reverse adverse effects.** Available in 2-, 5-, 10-, and 20-mL ampules in a concentration of 50 mcg/mL. A 10 mcg/mL dilution may be made by adding 1 mL of the 50 mcg/mL concentration to 4 mL preservative-free normal saline. Stable for 24 hours refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Alprostadil, amiodarone, atropine, caffeine citrate, cimetidine, dexamethasone, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, furosemide, heparin, hydrocortisone succinate, lidocaine, linezolid, lorazepam, metoclopramide, midazolam, milrinone, morphine, nafcillin, nicardipine, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanyl, and vecuronium.

**Incompatibility:** Azithromycin, pentobarbital and phenytoin.

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### Selected References

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- ◆ Fahnenstich H, Steffan J, Kau N, Bartmann P: Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. *Crit Care Med* 2000;28:836-839.
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- ◆ Product Information, Hospira, 2005

Compatibilities updated 7/2009

References updated 3/2008

Text updated 3/2002



### Dose & Administration

**IV:** 5 to 10 mcg/kg per dose IV over 15 seconds. May repeat every 45 seconds until the patient is awake. Maximum total cumulative dose should not exceed 50 mcg/kg (0.05 mg/kg) or 1 mg in infants, whichever is smaller (data in infants older than 1 year). No reported maximum dose in neonates has been tested. Administer intravenously through a freely running large vein to minimize pain upon injection.

**Intranasal:** 40 mcg/kg per dose divided equally between both nostrils. Administer via TB syringe for accurate equal dosing.

**Rectal:** 15 to 30 mcg/kg per dose, may repeat if sedation not reversed within 15 to 20 minutes.

### Uses

Reversal of sedative effect from benzodiazepines, in cases of suspected benzodiazepines overdose, and in neonatal apnea secondary to prenatal benzodiazepine exposure.

### Monitoring

Monitor for the return of sedation and respiratory depression. Continuous EKG and blood pressure.

### Adverse Effects/Precautions

The reported experience in neonates is very limited. Use with caution in neonates with pre-existing seizure disorders. Hypotension has been reported in adults following rapid administration. Resedation has been reported in 10% of treated pediatric patients, occurring 19 to 50 minutes after initial dosing. May cause pain on injection. Observe IV site for extravasation.

### Black Box Warning

According to the manufacturer's black box warning, the use of flumazenil has been associated with the occurrence of seizures. Seizures are most frequent in patients who have been on benzodiazepines for long-term sedation.

### Pharmacology

Imidazobenzodiazepine that is a benzodiazepine receptor antagonist. Competitively inhibits the activity at the benzodiazepine recognition site on the GABA/benzodiazepine receptor. Eliminated rapidly by hepatic metabolism to three inactive metabolites. Highly lipid soluble and penetrates the brain rapidly. Elimination half-life in children 20 to 75 minutes. Peak concentration reached in 3 minutes when delivered intravenously (children). Limited pharmacokinetic data in neonates.

### Special Considerations/Preparation

Available in an injectable form as a 0.1 mg/mL concentration in 5- and 10-mL multi-dose vials. If drawn into a syringe or mixed with D5W, LR, or NS, discard solution after 24 hours. Discard opened vials within 24 hours. Store at room temperature.

**Solution Compatibility:** D<sub>5</sub>W, Lactated Ringer's, and NS.

**Terminal Injection Site Compatibility:** Aminophylline, cimetidine, dobutamine, dopamine, famotidine, heparin, lidocaine, procainamide, and ranitidine.

*continued...*

### Selected References

- ♦ Phelps SJ, Hak EB: *Pediatric Injectable Drugs*. Maryland: American Society of Health System Pharmacists, 2004, p176.
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Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2007

Added 3/2005

Agustín Torres Mendoza  
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 ✍ CMP. 27344  
 RNE. 16790 - 19715  
 JEFE DE DPTO. PEDIATRÍA

**Dose & Administration**

**Note:** Fosphenytoin dosing is expressed in phenytoin equivalents (PE). (Fosphenytoin 1 mg PE = phenytoin 1 mg)

**Loading dose:** 15 to 20 mg PE/kg IM or IV infusion over at least 10 minutes.

**Maintenance dose:** 4 to 8 mg PE/kg every 24 hours IM or IV slow push. Begin maintenance 24 hours after loading dose.

Maximum rate of infusion 1.5 mg PE/kg per minute. May be administered more rapidly than phenytoin due to less infusion-related toxicity. Flush IV with saline before and after administration.

Term infants older than 1 week of age may require up to 8 mg PE/kg per dose every 8 to 12 hours.

**Uses**

Anticonvulsant. Generally used to treat seizures that are refractory to phenobarbital. Can be administered with lorazepam for rapid onset of seizure control.

**Monitoring**

Monitor blood pressure closely during infusion. Measure trough serum phenytoin (**not** fosphenytoin) concentration; obtain 48 hours after IV loading dose. Therapeutic serum phenytoin concentration: Probably 6 to 15 mcg/mL (up to 10 to 20 mcg/mL). Collect blood samples in EDTA tubes to minimize fosphenytoin to phenytoin conversion in the tube.

**Adverse Effects/Precautions**

Clinical signs of toxicity, such as drowsiness, are difficult to identify in infants, but are dose and infusion rate dependent. Minor venous irritation upon IV administration. Fosphenytoin drug interactions are similar to phenytoin (ie, carbamazepine, cimetidine, corticosteroids, digoxin, furosemide, phenobarbital, and valproate).

**FDA ALERT [11/24/08]:** FDA is investigating new preliminary data regarding a potential increased risk of serious skin reactions including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) from phenytoin therapy in Asian patients positive for a particular human leukocyte antigen (HLA) allele, HLA-B\*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais. Because fosphenytoin is a prodrug and is converted to phenytoin after administration, any concern regarding this association is also applicable to fosphenytoin.

**Use with caution in neonates with hyperbilirubinemia:** both fosphenytoin and bilirubin displace phenytoin from protein-binding sites, resulting in increased serum free phenytoin concentration.

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### Pharmacology

Fosphenytoin is a water-soluble prodrug of phenytoin rapidly converted by phosphatases in blood and tissue. It has no known intrinsic pharmacologic activity before conversion to phenytoin. Each 1.5 mg of fosphenytoin is metabolically converted to 1 mg phenytoin. Conversion half-life of fosphenytoin administered intravenously to young pediatric patients is approximately 7 minutes. Data obtained using spiked blood samples from term and preterm neonates demonstrated similar conversion rates. No drugs have been identified to interfere with the conversion of fosphenytoin to phenytoin. Fosphenytoin is highly protein bound (adults 95% to 99%) and does not penetrate the blood-brain barrier. Serum half-life reflects that of phenytoin (18 to 60 hours) due to rapid conversion. The conversion of fosphenytoin to phenytoin yields very small amounts of formaldehyde and phosphate. This is only significant in cases of large overdosage. Phenytoin serum concentrations measured up to two hours after IV and four hours after IM dose may be falsely elevated due to fosphenytoin interaction with immunoanalytic methods (eg, TDx fluorescence polarization).

### Special Considerations/Preparation

Available as an injectable solution in a concentration equivalent to 50 mg PE/mL, in 2- and 10-mL vials. Administer IM undiluted. Administer IV after diluting in NS or D<sub>5</sub>W to a concentration of 1.5 to 25 mg PE/mL. The pH is 8.6 to 9.0. **Store refrigerated.** Stable for 48 hours at room temperature. Do not use vials containing particulate matter.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W and NS.

**Terminal Injection Site Compatibility:** Lorazepam, phenobarbital, and potassium chloride.

**Incompatibility:** Midazolam.

### Selected References

- ◆ FDA Alert [11/24/08]. Information for Healthcare Professionals: Phenytoin and Fosphenytoin. Available at: [http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin\\_fosphenytoin-HCP.htm](http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoin-HCP.htm).
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- ◆ Product Information, Teva, 2007

Adverse Effects/Precautions and References updated 1/2009

NEOFAX® 2011

**Dose & Administration**

**Initial dose:** 10 mg/kg per dose every 24 hours IV or orally in the neonatal period, every 12 hours later in infancy.  
Adjust dosage upward as needed every 1 to 2 weeks to a maximum of 30 mg/kg per dose.

**Frequency:** Administer every 24 hours in the immediate neonatal period, every 12 hours later in infancy.

Administer IV slowly over 15 minutes. Dilute to a concentration of 5 mg/mL with a compatible diluent prior to administration.

**Uses**

Anticonvulsant. In the neonatal period, it has been used as a second line of therapy for seizures refractory to phenobarbital and other anticonvulsants.

**Monitoring**

Serum trough concentrations are not routinely monitored, although they may be useful when determining the magnitude of dosing adjustments. Therapeutic concentrations are approximately 10 to 40 mcg/mL.

**Adverse Effects/Precautions**

Data in neonates are limited to case reports and abstracts. Sedation and irritability have been reported in neonates and young infants. When discontinuing therapy, wean the dose gradually to minimize the potential of increased seizure frequency.

**Pharmacology**

Rapidly and completely absorbed after oral administration, with the onset of action by 30 minutes and peak concentration within 2 hours. Bioavailability is not affected by food. Half-life in the immediate neonatal period is approximately 18 hours, decreasing to 6 hours by 6 months of age. Minimal protein binding. Linear pharmacokinetics. Primarily (66%) excreted unchanged in the urine, with some metabolism via enzymatic hydrolysis to inactive metabolites (no cytochrome p450 involvement). Dose should be adjusted in patients with renal impairment. The precise mechanism of action is unknown. Levetiracetam inhibits burst firing without affecting normal neuronal excitability, suggesting that levetiracetam may selectively prevent hypersynchronization of epileptiform burst firing and propagation of seizure activity. There are no known significant drug interactions.

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**Special Considerations/Preparation**

Keppra® Injection for intravenous use is available in single-use 5 mL vials containing 500 mg (100 mg/mL). Keppra® Oral Solution is available in a concentration of 100 mg/mL (dye- and alcohol-free). Store both products at controlled room temperature.

**Solution Compatibility:** NS, Lactated Ringer's, and D<sub>5</sub>W.

**Terminal Injection Site Compatibility:** Lorazepam.

**Selected References**

- ◆ Shoemaker MT, Rotenberg JS: Levetiracetam for the treatment of neonatal seizures. *J Child Neurol* 2007;22:95-98.
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- ◆ De Smedt T, Raedt R, Vonck K, Boon P: Levetiracetam: Part II, the clinical profile of a novel anticonvulsant drug. *CNS Reviews* 2007;13:57-78.
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Added 3/2008

**Dose & Administration**

**Term, normothermic newborns:**

**Loading dose:** 2 mg/kg IV over 10 minutes, followed immediately by a

**Maintenance infusion:** 6 mg/kg per hour for 6 hours, then 4 mg/kg per hour for 12 hours, then 2 mg/kg per hour for 12 hours.

**Caution:** Preterm newborns and term newborns undergoing hypothermia treatment are at risk for drug accumulation due to slower drug clearance. Precise dosing in these infants is uncertain.

**Uses**

Treatment of severe recurrent or prolonged seizures that do not respond to first-line therapies.

**Monitoring**

Continuous monitoring of EKG, heart rate, and blood pressure. Observe for worsening of seizure activity. Measuring blood concentrations is not clinically useful except when accumulation is suspected.

**Adverse Effects/Precautions**

Do not use concurrently with phenytoin due to cardiac effects. Stop infusion immediately if significant cardiac arrhythmia occurs. Arrhythmias and significant bradycardia have occurred in 5% of reported cases. Slowing of the heart rate is common.

**Pharmacology**

The mode of action for lidocaine as an anticonvulsant drug is unknown. Lidocaine is metabolized in the liver into 2 active metabolites: monoethylglycinexylidide (MEGX) and glycinxylidide (GX). Approximately 30% is excreted unchanged in the urine. The half-life in neonates is at least 3 hours, and clearance is dose-dependent. The clinically effective dose of 6 mg/kg/hr will lead to accumulation of both lidocaine and metabolites within several hours. Free drug fraction in both term and premature neonates is approximately twice that found in older children because of significantly reduced protein binding by alpha 1-acid glycoprotein.

**Special Considerations/Preparation**

**Use only preservative-free lidocaine without epinephrine.** Available in multiple concentrations ranging from 1% to 20%. To make a dilution for bolus dosing, dilute 10 mg lidocaine (0.5 mL of 2% solution) in 9.5 mL NS or D<sub>5</sub>W, yielding a 1 mg/mL final concentration.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions, fat emulsion. Alteplase, aminophylline, amiodarone, ampicillin, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefoxitin, chloramphenicol, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, flumazenil, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, insulin, linezolid, metoclopramide, micafungin, morphine, nafcillin, nicardipine, nitroglycerin, penicillin G, pentobarbital, potassium chloride, procainamide, ranitidine, sodium bicarbonate, and sodium nitroprusside.

**Incompatibility:** Phenytoin.

*continued...*

**Selected References**

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Compatibilities updated 7/2009

Dose & Administration and References updated 1/2009

Added 3/2006



**Dose & Administration**

0.05 to 0.1 mg/kg per dose IV slow push. Repeat doses based on clinical response.

**Uses**

Anticonvulsant, acute management of patients with seizures refractory to conventional therapy.

**Monitoring**

Monitor respiratory status closely. Observe IV site for signs of phlebitis or extravasation.

**Adverse Effects/Precautions**

Respiratory depression. Rhythmic myoclonic jerking has occurred in premature neonates receiving lorazepam for sedation.

**Pharmacology**

Dose-dependent CNS depression. Onset of action within 5 minutes; peak serum concentration within 45 minutes. Duration of action is 3 to 24 hours. Mean half-life in term neonates is 40 hours. Metabolized to an inactive glucuronide, which is excreted by the kidneys. Highly lipid-soluble.

**Special Considerations/Preparation**

Limited data are available for neonates. Available in 2-mg/mL and 4-mg/mL concentrations (1 mL preservative free vial) and 2 mg/mL multidose vial (10 mL). Some available products contain 2% (20 mg/mL) benzyl alcohol and 18% polyethylene glycol 400 in propylene glycol. A dilution of 0.4 mg/mL may be prepared by adding 1 mL of 4 mg/mL concentration in 9 mL of preservative-free sterile water for injection. This will make it easier to measure the dose and decrease the benzyl alcohol content to 0.5 mg/kg per dose. Solutions should not be used if they are discolored or contain a precipitate.

**Solution Compatibility:** D<sub>5</sub>W, NS, and sterile water for injection.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, amiodarone, bumetanide, cefepime, cefotaxime, cimetidine, dexamethasone, dobutamine, dopamine, epinephrine, erythromycin lactobionate, famotidine, fentanyl, fluconazole, fosphenytoin, furosemide, gentamicin, heparin, hydrocortisone succinate, labetalol, levetiracetam, linezolid, methadone, metronidazole, midazolam, milrinone, morphine, nicardipine, nitroglycerin, pancuronium bromide, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanyl, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, and zidovudine.

**Incompatibility:** Fat emulsion. Aztreonam, caffeine citrate, and imipenem/cilastatin.

*continued...*

**Selected References**

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- ◆ Deshmukh A, Wittert W, Schnitzler E, Mangurten HH: Lorazepam in the treatment of refractory neonatal seizures. *Am J Dis Child* 1986;140:1042.
- ◆ Product Information, Bedford, 2004

Compatibilities updated 7/2009

**Dose & Administration**

**Initial dose:** 0.05 to 0.2 mg/kg per dose every 12 to 24 hours orally. Reduce dose by 10% to 20% per week over 4 to 6 weeks. Adjust weaning schedule based on signs and symptoms of withdrawal.

**Uses**

Treatment of neonatal abstinence syndrome and opioid dependence.

**Monitoring**

Monitor respiratory and cardiac status closely. A 12-lead ECG should be obtained on methadone-exposed infants experiencing bradycardia or tachycardia. Assess for gastric residuals, abdominal distention, and loss of bowel sounds.

**Adverse Effects/Precautions**

Respiratory depression in excessive doses. Ileus and delayed gastric emptying. In a single case report, QTc prolongation was noted in a term infant born to a mother receiving methadone maintenance therapy (50 mg/day). After birth, the infant's resting HR was 80 to 90 beats per minute and ECG showed a QTc of 510 ms. This resolved spontaneously over 5 days.

**Black Box Warning**

According to the manufacturer's black box warning, deaths have been reported during initiation of methadone treatment for opioid dependence. In some cases, deaths appear to have occurred due to respiratory or cardiac effects of methadone and too-rapid titration without appreciation for the accumulation of methadone over time. It is critical to understand the pharmacokinetics of methadone and to exercise vigilance during treatment initiation and dose titration. Respiratory depression is the chief hazard associated with methadone, and its peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. Cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed (in adults). Most cases involve (adult) patients being treated for pain with large, multiple daily doses, although cases have been reported in patients receiving doses used for maintenance treatment of opioid addiction. Special requirements for dispensing exist, and the oral solution must not be injected.

**Pharmacology**

Long-acting narcotic analgesic. Oral bioavailability is 50%, with peak plasma levels obtained in 2 to 4 hours. Metabolized extensively via hepatic N-demethylation. Highly protein bound (90% adults). Serum half-life ranges from 16 to 25 hours in neonates and is prolonged in patients with renal failure. Rifampin and phenytoin accelerate the metabolism of methadone and can precipitate withdrawal symptoms.

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**Special Considerations/Preparation**

Available as oral solutions in 1- and 2-mg/mL concentrations containing 8% alcohol, and a 10-mg/mL alcohol-free solution. May dilute 1 mL of the 10-mg/mL concentrated solution with 19 mL of sterile water to provide an oral dilution with a final concentration of 0.5 mg/mL. Stable for 24 hours refrigerated. Also available as 5- and 10-mg tablets.

**Solution Compatibility:** NS.

**Terminal Injection Site Compatibility:** Atropine sulfate, dexamethasone, lorazepam, metoclopramide, midazolam, and phenobarbital.

**Incompatibility:** Phenytoin.

**Selected References**

- ♦ Burgos AE, Burke Jr. BL: Neonatal abstinence syndrome. *NeoReviews* 2009;10:e222-e229.
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- ♦ Hussain T, Ewer AK: Maternal methadone may cause arrhythmias in neonates. *Acta Paediatr* 2007;96:768-769.
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- ♦ Tobias JD, Schleien CL, Haun SE: Methadone as treatment for iatrogenic narcotic dependency in pediatric intensive care unit patients. *Crit Care Med* 1990;18:1292.
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- ♦ Rosen TS, Pippenger CE: Pharmacologic observations on the neonatal withdrawal syndrome. *J Pediatr* 1976;88:1044.
- ♦ Product Information, Roxane, 2007

Uses, Compatibilities, and References updated 7/2009

Adverse Effects/Precautions, Monitoring and References updated 3/2009

### Dose & Administration

**Sedation:**

**IV:** 0.05 to 0.15 mg/kg **over at least 5 minutes**. Repeat as required, usually every 2 to 4 hours. May also be given IM. Dosage requirements are decreased by concurrent use of narcotics.

**Continuous IV infusion:** 0.01 to 0.06 mg/kg per hour (10 to 60 mcg/kg/hour). Dosage may need to be increased after several days of therapy because of development of tolerance and/or increased clearance.

**Intranasal:** 0.2 to 0.3 mg/kg per dose using 5-mg/mL injectable form.

**Sublingual:** 0.2 mg/kg per dose using 5-mg/mL injectable form mixed with a small amount of flavored syrup.

**Oral:** 0.25 mg/kg per dose using Versed® oral syrup.

**Anticonvulsant:**

**Loading dose:** 0.15 mg/kg (150 mcg/kg) IV over at least 5 minutes, followed by

**Maintenance infusion:** 0.06 to 0.4 mg/kg per hour (1 to 7 mcg/kg per minute).

### Uses

Sedative/hypnotic. Anesthesia induction. Treatment of refractory seizures.

### Monitoring

Follow respiratory status and blood pressure closely, especially when used concurrently with narcotics. Assess hepatic function. Observe for signs of withdrawal after discontinuation of prolonged therapy.

### Adverse Effects/Precautions

**Black Box Warning**

According to the manufacturer's black box warning, midazolam has been associated with respiratory depression and respiratory arrest, especially when used for sedation in noncritical care settings. Doses should be titrated slowly. Midazolam should not be given by rapid injection in the neonatal population, as severe hypotension and seizures have been reported.

Respiratory depression and hypotension are common when used in conjunction with narcotics, or following rapid bolus administration. Seizure-like myoclonus has been reported in 8% of premature infants receiving continuous infusions - this also may occur following rapid bolus administration and in patients with underlying CNS disorders. Nasal administration may be uncomfortable because of a burning sensation.

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**Pharmacology**

Relatively short-acting benzodiazepine with rapid onset of action. Sedative and anticonvulsant properties related to GABA accumulation and occupation of benzodiazepine receptor. Antianxiety properties related to increasing the glycine inhibitory neurotransmitter. Metabolized by hepatic CYP 3A4 to a less active hydroxylated metabolite, then glucuronidated before excretion in urine. Drug accumulation may occur with repeated doses, prolonged infusion therapy, or concurrent administration of cimetidine, erythromycin or fluconazole. Highly protein bound. Duration of action is 2 to 6 hours. Elimination half-life is approximately 4 to 6 hours in term neonates, and quite variable, up to 22 hours, in premature babies and those with impaired hepatic function. Bioavailability is approximately 36% with oral administration and 50% with sublingual and intranasal administration. Midazolam is water soluble in acidic solutions and becomes lipid soluble at physiologic pH.

**Special Considerations/Preparation**

A preservative-free preparation is available as 1- and 5-mg/mL concentrations in 1-, 2-, and 5-mL vials.

Versed® is available in an injectable form as 1- and 5-mg/mL concentrations in 1-, 2-, 5-, and 10-mL vials. Contains 1% (10mg/mL) benzyl alcohol as a preservative. To decrease benzyl alcohol content, a 0.5 mg/mL dilution may be made by adding 1 mL of the 5-mg/mL concentration to 9 mL preservative-free sterile water for injection. Dilution stable for 24 hours refrigerated.

Versed® oral syrup is available in a 2 mg/mL concentration. Store at room temperature.

**Solution Compatibility:** D<sub>5</sub>W, NS, and sterile water for injection.

**Terminal Injection Site Compatibility:** Dex/AA solutions (midazolam 0.5 mg/mL or less; concentrations greater than 0.5 mg/mL incompatible). Amikacin, aminophylline, amiodarone, atropine, calcium gluconate, cefazolin, cefotaxime, cimetidine, clindamycin, digoxin, dobutamine, dopamine, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, gentamicin, glycopyrrolate, heparin, imipenem/cilastatin, insulin, linezolid, lorazepam, methadone, metoclopramide, metronidazole, milrinone, morphine, nifedipine, nitroglycerin, nitroprusside, pancuronium bromide, piperacillin, potassium chloride, propofol, ranitidine, remifentanyl, theophylline, tobramycin, vancomycin, and vecuronium.

**Incompatibility:** Fat emulsion. Albumin, ampicillin, bumetanide, cefepime, ceftazidime, dexamethasone, fosphenytoin, furosemide, hydrocortisone succinate, micafungin, nafcillin, and sodium bicarbonate.

*continued...*

## Selected References

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- ◆ Product Information, Hospira, 2004.

Compatibilities and References updated 12/2010

Dose & Administration and Adverse Effects/Precautions updated 1/2009

Pharmacology updated 3/2003





**Dose & Administration**

0.05 to 0.2 mg/kg per dose IV over at least 5 minutes, IM, or subQ. Repeat as required (usually every 4 hours).

**Continuous infusion:** Give a loading dose of 0.1 to 0.15 mg/kg over 1 hour followed by 0.01 to 0.02 mg/kg per hour.

**Treatment of opioid dependence:** Begin at most recent IV morphine dose equivalent. Taper 10% to 20% per day as tolerated. Oral dose is approximately 3 to 5 times IV dose.

**Initial treatment of neonatal abstinence syndrome:** 0.03 to 0.1 mg/kg per dose orally every 3 to 4 hours. Wean dose by 10% to 20% every 2 to 3 days based on abstinence scoring. Use a 0.4-mg/mL dilution made from a concentrated oral morphine sulfate solution.

**Uses**

Analgesia. Sedation. Treatment of opioid dependence and neonatal abstinence syndrome.

**Monitoring**

Monitor respiratory and cardiovascular status closely. Observe for abdominal distention and loss of bowel sounds. Consider urine retention if output is decreased.

**Adverse Effects/Precautions**

Naloxone should be readily available to reverse adverse effects. Marked respiratory depression (decreases the responsiveness of the respiratory center to CO<sub>2</sub> tension). Hypotension and bradycardia. Transient hypertonia. Ileus and delayed gastric emptying. Urine retention. Tolerance may develop after prolonged use; wean slowly. Seizures reported in two infants who received bolus plus infusion.

**Pharmacology**

Morphine is a narcotic analgesic that stimulates brain opioid receptors. Increases venous capacitance, caused by release of histamine and central suppression of adrenergic tone. GI secretions and motility decreased. Increases smooth muscle tone. Morphine is converted in the liver to two glucuronide metabolites (morphine-6-glucuronide and morphine-3-glucuronide) that are renally excreted. Morphine-6-glucuronide (M6G) is a potent respiratory-depressant and analgesic. Morphine-3-glucuronide (M3G) is an antagonist to the effects of morphine and morphine-6-glucuronide. Morphine is 20% to 40% bioavailable when administered orally. Pharmacokinetics are widely variable. Elimination half-life is approximately 9 hours for morphine and 18 hours for morphine-6-glucuronide. Steady state concentrations of morphine are reached by 24 to 48 hours.

**Special Considerations/Preparation**

Injectable solutions are available in dosage strengths ranging from 0.5- to 50-mg/mL.

Oral morphine sulfate solutions are available in concentrations of 2, 4, and alcohol-free 20 mg/mL.

A 0.4-mg/mL oral morphine dilution may be made by adding 1 mL of the 4-mg/mL injectable solution to 9 mL preservative-free normal saline. Stable for 7 days refrigerated. **Protect from light.**

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**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

For continuous infusions of morphine **containing heparin:** Use only NS; maximum morphine concentration 5 mg/mL.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, alteplase, amikacin, aminophylline, amiodarone, ampicillin, atropine, aztreonam, bumetanide, caffeine citrate, calcium chloride, caspofungin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cefazolin, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, furosemide, gentamicin, glycopyrrolate, heparin, hydrocortisone succinate, ibuprofen lysine, insulin, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, metronidazole, mezlocillin, midazolam, milrinone, nafcillin, nifedipine, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, propranolol, ranitidine, remifentanyl, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, and zidovudine.

**Incompatibility:** Azithromycin, cefepime, micafungin, pentobarbital, and phenytoin.

**Selected References**

- ◆ Burgos AE, Burke Jr. BL: Neonatal abstinence syndrome. *NeoReviews* 2009;10:e222-2229.
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- ◆ Oei J, Lui K: Management of the newborn infant affected by maternal opiates and other drugs of dependency. *J Paediatr Child Health* 2007;43:9-18.
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- ◆ Chay PCW, Duffy BJ, Walker JS: Pharmacokinetic-pharmacodynamic relationships of morphine in neonates. *Clin Pharmacol Ther* 1992;51:334.
- ◆ Koren G, Butt W, Chinyanga H, et al: Postoperative morphine infusion in newborn infants: Assessment of disposition characteristics and safety. *J Pediatr* 1985;107:963.
- ◆ Product Information, Mayne, 2004

Compatibilities updated 10/2009

Uses, Compatibilities, and References updated 7/2009

Dose updated 3/2007

### Dose & Administration

**Suggested dose:** 0.1 mg/kg IV push.

Doses needed to reverse narcotic-induced depression may be as low as 0.01 mg/kg.

May give IM if adequate perfusion. Tracheal administration is not recommended.

There are no studies to support or refute the current dosing recommendations.

### Uses

Narcotic antagonist. Adjuvant therapy to customary resuscitation efforts for narcotic-induced respiratory (CNS) depression. Naloxone is not recommended as part of the initial resuscitation of newborns with respiratory depression in the delivery room. Before naloxone is given, providers should restore heart rate and color by supporting ventilation.

### Monitoring

Assess respiratory effort and neurologic status.

### Adverse Effects/Precautions

No short-term toxicity observed. One case report of seizures secondary to acute opioid withdrawal after administration to an infant born to an opioid abuser. Long-term safety has not been investigated.

### Pharmacology

Reverses respiratory depression by competing for CNS narcotic receptor sites. Onset of action is variable, but usually within minutes after IV administration, and approximately 1 hour after IM administration. Half-life in neonates is approximately 70 minutes. Metabolized by the liver and excreted in the urine. Increases circulating catecholamines.

### Special Considerations/Preparation

**Do not mix in an alkaline solution.** Available in 0.4 mg/mL (1-mL fill in 2-mL Carpuject® cartridge) and 1-mg/mL concentrations. **Store at room temperature and protect from light.**

**Solution Compatibility:** NS and D<sub>5</sub>W. No data are currently available on Dex/AA.

**Terminal Injection Site Compatibility:** Heparin, linezolid, and propofol.

No data are currently available on potassium chloride and other medications.

### Selected References

- ◆ Perlman JM, Wyllie J, Kattwinkel J, et al on behalf of the Neonatal Resuscitation Chapter Collaborators. Part 11: neonatal resuscitation: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation* 2010;122(suppl 2):S516-S538.
- ◆ Guinsburg R, Wyckoff MH. Naloxone during neonatal resuscitation: acknowledging the unknown. *Clin Perinatol* 2006;33:121-132.
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- ◆ Product Information, Hospira, 2008.

Special Considerations, Compatibilities, and References updated 12/2010

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**Dose & Administration**

**Myasthenia gravis:** 0.1 mg IM (give 30 minutes before feeding).  
1 mg orally (give 2 hours before feeding). Dose may have to be increased and should be titrated.

**Reversal of neuromuscular blockade:** 0.04 to 0.08 mg/kg IV, in addition to atropine 0.02 mg/kg.

**Uses**

Neonatal transient myasthenia gravis. Neonatal persistent (congenital) myasthenia gravis. Reversing effects of neuromuscular blocking drugs.

**Monitoring**

Monitor respiratory and cardiovascular status closely.

**Adverse Effects/Precautions**

Contraindicated in presence of intestinal or urinary obstruction, bradycardia, or hypotension. Use cautiously in patients with bronchospasm or cardiac arrhythmia. Adverse effects include muscle weakness, tremors, bradycardia, hypotension, respiratory depression, bronchospasm, diarrhea, and excessive salivation.

**Pharmacology**

Inhibits acetylcholinesterase at the neuromuscular junction, allowing accumulation of acetylcholine and thus restoring activity.

**Special Considerations/Preparation**

Available as injectable solution in 1-mL ampules and 10-mL vials in concentrations of 1:1000 (1 mg/mL) and 1:2000 (0.5 mg/mL). **Protect from light.**

**Solution Compatibility:** No data.

**Terminal Injection Site Compatibility:** Glycopyrrolate, heparin, hydrocortisone succinate, netilmicin, pentobarbital and potassium chloride.

**Selected References**

- ♦ Fisher DM, Cronnelly R, Miller RD, Sharma M: The neuromuscular pharmacology of neostigmine in infants and children. *Anesthesiology* 1983;59:220.
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- ♦ Product Information, Abraxis, 2006

Compatibilities updated 7/2009

Text updated 3/2001

**Dose & Administration**

0.1 mg/kg (0.04 to 0.15 mg/kg) IV push, as needed for paralysis. Usual dosing interval is 1 to 2 hours. Adjust dose as needed based on duration of paralysis.

**Uses**

Skeletal muscle relaxation/paralysis in infants requiring mechanical ventilation. Proposed desirable effects are improved oxygenation/ventilation, reduced barotrauma, and reduced fluctuations in cerebral blood flow.

**Monitoring**

Monitor vital signs frequently, blood pressure continuously. Use some form of eye lubrication.

**Adverse Effects/Precautions**

Hypoxemia may occur because of inadequate mechanical ventilation and deterioration in pulmonary mechanics. Tachycardia and blood pressure changes (both hypotension and hypertension) occur frequently. Increased salivation.

**Black Box Warning**

According to the manufacturer's black box warning, pancuronium should be administered by adequately trained individuals familiar with its actions, characteristics, and hazards.

**Pharmacology**

Nondepolarizing muscle-relaxant that competitively antagonizes autonomic cholinergic receptors and also causes sympathetic stimulation. Partially hydroxylated by the liver, 40% excreted unchanged in urine. Onset of action is 1 to 2 minutes; duration varies with dose and age. Reversed by neostigmine and atropine.

Factors affecting duration of neuromuscular blockade:

**Potential:** Acidosis, hypothermia, neuromuscular disease, hepatic disease, renal failure, cardiovascular disease, younger age, aminoglycosides, hypermagnesemia, and hypokalemia.

**Antagonism:** Alkalosis, epinephrine, and hyperkalemia.

Sensation remains intact; analgesia should be used for painful procedures.

**Special Considerations/Preparation**

Available in concentrations of 1-mg/mL (10 mL vials) and 2-mg/mL (2- and 5-mL vials). Products contain 1% (10 mg/mL) benzyl alcohol. **Refrigerate.**

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Aminophylline, caffeine citrate, cefazolin, cimetidine, dobutamine, dopamine, epinephrine, esmolol, fentanyl, fluconazole, gentamicin, heparin, hydrocortisone succinate, isoproterenol, lorazepam, midazolam, milrinone, morphine, nitroglycerin, nitroprusside, propofol, ranitidine, trimethoprim-sulfamethoxazole, and vancomycin.

**Incompatibility:** Pentobarbital and phenobarbital.

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**Selected References**

- ◆ Bhutani VK, Abbasi S, Sivieri EM: Continuous skeletal muscle paralysis: Effect on neonatal pulmonary mechanics. *Pediatrics* 1988;81:419.
- ◆ Costarino AT, Polin RA: Neuromuscular relaxants in the neonate. *Clin Perinatol* 1987;14:965.
- ◆ Cabal LA, Siassi B, Artal R, et al: Cardiovascular and catecholamine changes after administration of pancuronium in distressed neonates. *Pediatrics* 1985;75:284.
- ◆ Product Information, Sico, 2003

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

Text updated 1/1993

**Dose & Administration**

2 to 6 mg/kg IV slow push.

**Uses**

Sedative/hypnotic, for short-term use.

**Monitoring**

Monitor respiratory status and blood pressure closely. Serum concentration for sedation: 0.5 to 3 mcg/mL.

**Adverse Effects/Precautions**

Respiratory depression. Tolerance, dependence, and cardiovascular depression occur with continued use. Enhances metabolism of phenytoin, sodium valproate, and corticosteroids by microsomal enzyme induction.

**Pharmacology**

Short-acting barbiturate. Pentobarbital has no analgesic effects. Serum half-life is dose-dependent (15 to 50 hours in adults) and unknown in neonates. Metabolized by hepatic microsomal enzyme system.

**Special Considerations/Preparation**

Available as a 50-mg/mL solution in 20 mL and 50 mL multidose vials. Solution contains propylene glycol 40%, and alcohol 10%. Irritating to veins; pH is 9.5.

A 5-mg/mL dilution may be made by adding 1 mL of the 50-mg/mL solution to 9 mL of preservative-free normal saline. Use immediately.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA Solutions. Acyclovir, amikacin, aminophylline, atropine, calcium chloride, chloramphenicol, erythromycin lactobionate, hyaluronidase, insulin, lidocaine, linezolid, neostigmine, and propofol.

**Incompatibility:** Fat emulsion. Cimetidine, fentanyl, hydrocortisone succinate, midazolam, morphine, pancuronium bromide, penicillin G, phenytoin, ranitidine, and vancomycin. No data are currently available on heparin and potassium chloride.

**Selected References**

- ♦ Strain JD, Harvey LA, Foley LC, Campbell JB: Intravenously administered pentobarbital sodium for sedation in pediatric CT. *Radiology* 1986;161:105.
- ♦ Product Information, Ovation, 2005

Compatibilities updated 7/2009

Text updated 3/1997





**Dose & Administration****Anticonvulsant:**

**Loading dose:** 20 mg/kg IV, given slowly over 10 to 15 minutes.

**Refractory seizures:** Additional 5-mg/kg doses, up to a total of 40 mg/kg.

**Maintenance:** 3 to 4 mg/kg per day beginning 12 to 24 hours after the load.

**Frequency/Route:** Daily (every 12 hours probably unnecessary). IV slow push (most rapid control of seizures), IM, orally, or rectally.

**Neonatal Abstinence Syndrome:**

**Loading dose:** 16 mg/kg orally on day 1.

**Maintenance:** 1 to 4 mg/kg per dose orally every 12 hours.

Based on abstinence scoring, weaning can be achieved by decreasing dose 20% every other day.

**Uses**

Anticonvulsant. May improve outcomes in severely asphyxiated infants (40 mg/kg IV infusion over 1 hour, prior to onset of seizures).

Neonatal abstinence syndrome in nonopiate- or polydrug-exposed infants.

May enhance bile excretion in patients with cholestasis before <sup>99</sup>Tc-IDA scanning.

**Monitoring**

Phenobarbital monotherapy will control seizures in 43% to 85% of affected neonates - adding a second drug (phenytoin or lorazepam) is often needed. Therapeutic serum concentration is 15 to 40 mcg/mL. Drug accumulation may occur using recommended maintenance dose during the first two weeks of life. Altered (usually increased) serum concentrations may occur in patients also receiving phenytoin or valproate. Observe IV site for signs of extravasation and phlebitis. In infants with neonatal abstinence syndrome, serum concentrations of 20 to 30 mcg/mL are associated with adequate symptom control.

**Adverse Effects/Precautions**

Sedation at serum concentrations above 40 mcg/mL. Respiratory depression at concentrations above 60 mcg/mL. Irritating to veins - pH is approximately 10 and osmolality is approximately 15,000 mOsm/kg H<sub>2</sub>O.

**Pharmacology**

Phenobarbital limits the spread of seizure activity, possibly by increasing inhibitory neurotransmission. Approximately 30% protein bound. Primarily metabolized by liver, then excreted in the urine as p-hydroxyphenobarbital (no anticonvulsant activity). Serum half-life in neonates is 40 to 200 hours.

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**Special Considerations/Preparation**

Injectable solution available in concentrations of 60-, 65-, and 130-mg/mL, all containing 10% (100 mg/mL) alcohol and 67.8% propylene glycol.

Oral elixir is available in 20 mg/5 mL concentration.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA Solutions. Amikacin, aminophylline, caffeine citrate, calcium chloride, calcium gluconate, enalaprilat, fentanyl, fosphenytoin, heparin, ibuprofen lysine, linezolid, meropenem, methadone, morphine, propofol, and sodium bicarbonate.

**Incompatibility:** Fat emulsion. Hydralazine, hydrocortisone succinate, insulin, methadone, pancuronium, ranitidine, and vancomycin. No data available on potassium chloride.

**Selected References**

- ◆ Burgos AE, Burke Jr. BL: Neonatal abstinence syndrome. *NeoReviews* 2009;10:e222-e229.
- ◆ Volpe JJ: *Neurology of the Newborn*, ed 4. Philadelphia: WB Saunders Co, 2001, p 203-204.
- ◆ Hall RT, Hall FK, Daily SK: High-dose phenobarbital therapy in term newborn infants with severe perinatal asphyxia: A randomized, prospective study with three-year follow-up. *J Pediatr* 1998;132:345-348.
- ◆ Finnegan LP, Michael H, Leifer B, Desai S: An evaluation of neonatal abstinence treatment modalities. *NIDA Res Monogr* 1984;49:282-288.
- ◆ Finnegan LP, Mitros TF, Hopkins LE: Management of neonatal narcotic abstinence utilizing a phenobarbital loading dose method. *NIDA Res Monogr* 1979;27:247-253.
- ◆ Product Information, PAI, 2005
- ◆ Product Information, Hospira, 2004

Compatibilities updated 10/2009

Dose & Administration, Uses, Monitoring, Compatibility, and References updated 7/2009

Text updated 3/2002

**Dose & Administration**

**Loading dose:** 15 to 20 mg/kg IV infusion over at least 30 minutes.

**Maintenance dose:** 4 to 8 mg/kg every 24 hours IV slow push, or orally.

(Up to 8 mg/kg per dose every 8 to 12 hours after 1 week of age).

Maximum rate of infusion 0.5 mg/kg per minute. Flush IV with saline before and after administration. **Phenytoin is highly unstable in any IV solution. Avoid using in central lines because of the risk of precipitation. IM route not acceptable; drug crystallizes in muscle.** Oral absorption is erratic.

**Uses**

Anticonvulsant often used to treat seizures refractory to phenobarbital.

**Monitoring**

Monitor for bradycardia, arrhythmias, and hypotension during infusion. Observe IV site for extravasation. Follow serum concentration closely; therapeutic range is 6 to 15 mcg/mL in the first weeks, then 10 to 20 mcg/mL due to changes in protein binding. Obtain initial trough level 48 hours after IV loading dose.

**Adverse Effects/Precautions**

Extravasation causes tissue inflammation and necrosis due to high pH and osmolality. High serum concentrations are associated with seizures. Drowsiness may be difficult to identify. Hypersensitivity reactions have been reported in infants. Toxicities with long-term therapy include cardiac arrhythmias, hypotension, gingivitis, nystagmus, rickets, hyperglycemia, and hypoinsulinemia. Phenytoin interacts with carbamazepine, cimetidine, corticosteroids, digoxin, furosemide, phenobarbital, and valproate.

**FDA ALERT [11/24/08]:** FDA is investigating new preliminary data regarding a potential increased risk of serious skin reactions including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) from phenytoin therapy in Asian patients positive for a particular human leukocyte antigen (HLA) allele, HLA-B\*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais.

**Pharmacology**

Hepatic metabolism capacity is limited; saturation may occur within therapeutic range. Pharmacokinetics are dose-dependent. Elimination rate is increased during first few weeks of life. Serum half-life is 18 to 60 hours. 85% to 90% protein bound. Bilirubin displaces phenytoin from protein-binding sites, resulting in increased free drug.

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**Special Considerations/Preparation**

Injectable solution available in a concentration of 50 mg/mL. Contains 40% propylene glycol and 10% alcohol (100 mg/mL).  
Oral suspension available in a concentration of 25 mg/mL.

**Solution Compatibility:** Phenytoin is highly unstable in any IV solution.

**Solution Incompatibility:** D<sub>5</sub>W and D<sub>10</sub>W.

**Terminal Injection Site Compatibility:** Esmolol, famotidine, and fluconazole.

**Incompatibility:** Dex/AA solutions, fat emulsion. Amikacin, cefepime, ceftazidime, chloramphenicol, clindamycin, dobutamine, enalaprilat, fentanyl, heparin, hyaluronidase, hydrocortisone succinate, insulin, lidocaine, linezolid, methadone, micafungin, morphine, nitroglycerin, pentobarbital, potassium chloride, procainamide, propofol, sodium bicarbonate, and vitamin K<sub>1</sub>.

**Selected References**

- ◆ FDA Alert [11/24/08]. Information for Healthcare Professionals: Phenytoin and Fosphenytoin. Available at: [http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin\\_fosphenytoinHCP.htm](http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoinHCP.htm).
- ◆ Volpe JJ: *Neurology of the Newborn*, ed 4. Philadelphia: WB Saunders Co, 2001, p 204-205.
- ◆ Wheless JW: Pediatric use of intravenous and intramuscular phenytoin: lessons learned. *J Child Neurol* 1998;13(Suppl 1): S11-14.
- ◆ Product Information, Hospira, 2004
- ◆ Product Information, Pfizer, 2006

Compatibilities updated 7/2009

Adverse Effects/Precautions and References updated 1/2009

Text updated 3/2002

**Dose & Administration**

0.3 to 0.6 mg/kg per dose IV push over 5 to 10 seconds. Do not give IM.

Must be accompanied by adequate analgesia and/or sedation.

**Uses**

Skeletal muscle relaxation/paralysis in infants requiring endotracheal intubation.

**Monitoring**

Assess vital signs frequently and blood pressure continuously if possible.

**Adverse Effects/Precautions**

The use of rocuronium in infants has only been studied in patients under halothane anesthesia. The overall analysis of ECG data in pediatric patients indicates that the concomitant use of rocuronium with general anesthetic agents can prolong the QTc interval. Most pediatric patients anesthetized with halothane who did not receive atropine for induction experienced a transient increase (30% or greater) in heart rate after intubation, whereas only 1 of 19 infants anesthetized with halothane and fentanyl who received atropine for induction experienced this magnitude of change. Aminoglycosides, vancomycin, and hypermagnesemia may enhance neuromuscular blockade. Propofol has no effect. Phenytoin may diminish neuromuscular blockade. Respiratory and metabolic acidosis prolong the recovery time, respiratory alkalosis shortens it. Rocuronium may be associated with increased pulmonary vascular resistance, so caution is appropriate in patients with pulmonary hypertension. Extravasations cause local tissue irritation. The package insert statement that rocuronium is not recommended for rapid sequence intubations in pediatric patients is due to the lack of studies.

**Pharmacology**

Rocuronium is an aminosteroid nondepolarizing neuromuscular blocking agent that is an analog of vecuronium with 10% to 15% of its potency. It has a rapid to intermediate onset depending on dose and intermediate duration. It acts by competing for cholinergic receptors at the motor end-plate. This action is antagonized by acetylcholinesterase inhibitors, such as neostigmine and edrophonium. Plasma levels of rocuronium follow a three compartment open model following intravenous administration. The rapid distribution half-life is 1 to 2 minutes and the slower distribution half-life is 14 to 18 minutes. Onset of clinical effect usually occurs within 2 minutes and the duration ranges from 20 minutes to 2 hours. Larger doses (0.9 to 1.2 mg/kg) lead to more rapid onset and longer duration of clinical effect. It can have differential effects on various muscle groups (eg, laryngeal vs adductor pollicis vs diaphragm). The onset of laryngeal adductor paralysis is significantly slower with rocuronium compared with succinylcholine. Despite this difference, rocuronium has the fastest onset of any currently available nondepolarizing muscle relaxant. Average half-life in newborns is 1.1 hours. Rocuronium is approximately 30% protein bound, and is primarily excreted by the liver. There are no known metabolites.

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**Special Considerations/Preparation**

Zemuron® for intravenous injection is available in 5 mL and 10 mL multiple-dose vials containing 10 mg/mL. Each mL contains 10 mg rocuronium bromide and 2 mg sodium acetate. The solution is clear, colorless to yellow/orange, and is adjusted to isotonicity with sodium chloride and to a pH of 4 with acetic acid and/or sodium hydroxide. Store refrigerated, 2 to 8 degrees C (36 to 46 degrees F). DO NOT FREEZE. Upon removal from refrigeration to room temperature storage conditions (25 degrees C/77 degrees F), use within 60 days. Use opened vials within 30 days.

To prepare a 1 mg/mL solution, dilute 1 mL of the 10 mg/mL solution up to a final volume of 10 mL with NS. Dilution stable for 24 hours.

**Solution Compatibility:** D<sub>5</sub>W, Lactated Ringer's, and NS.

**Terminal Injection Site Compatibility:** Milrinone.

**Incompatibility:** Micafungin.

**Selected References**

- ◆ Perry JJ, Lee JS, Sillberg VAH, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database of Systematic Reviews* 2008, Issue 2, Art. No.: CD002788. DOI:10.1002/14651858.CD002788.pub2.
- ◆ Rapp H-J, Altenmueller CA, Waschke C: Neuromuscular recovery following rocuronium bromide single dose in infants. *Pediatr Anesthes* 2004; 14:329-355.
- ◆ Eikermann M, Hunkemöller I, Peine L, et al: Optimal rocuronium dose for intubation during inhalation induction with sevoflurane in children. *Br J Anaesthaes* 2002;89:277-281.
- ◆ Sparr HJ, Beaufort TM, Fuchs-Buder T: Newer neuromuscular blocking agents: how do they compare with established agents. *Drugs* 2001;61:919-942.
- ◆ Product information, Schering, 2008.

Added 3/2009

**Dose & Administration**

**Preterm infants:** 0.5 to 1 mL of 12% to 24% sucrose solution.

**Term infants:** 2 mL of 12% to 24% sucrose solution.

Administer sucrose solution directly to the tongue 2 minutes prior to the painful procedure.

For patients able to suck, a pacifier should be offered immediately after sucrose administration.

Alternatively, a pacifier dipped in sucrose solution can be offered 2 minutes prior to the procedure.

**Uses**

Mild analgesia and behavioral comforting.

**Monitoring**

Assess for signs of pain and discomfort.

**Adverse Effects/Precautions**

Sucrose 24% has an osmolarity of approximately 1000 mOsm/L. The adverse effects of repeated doses in premature infants are unknown.

**Pharmacology**

Sucrose administration provides a calming effect and reduces acute procedural pain in both preterm and term infants. The potential mechanism of these effects includes activation of the endogenous opioid system through taste receptors on the tip of the tongue. The time to maximal effect is approximately 2 minutes and the duration of effect is approximately 5 to 10 minutes. The beneficial effects of sucrose can be improved by nonnutritive sucking.

**Special Considerations/Preparation**

Sweet-Ease®, a 24% sucrose and water solution, is aseptically packaged in an 15 ml cup with a peel off lid that is suitable for dipping a pacifier or for administration via a dropper.

*continued...*

### Selected References

- ◆ Lefrak L, Burch K, Caravantes R, et al: Sucrose analgesia: Identifying potentially better practices. *Pediatrics* 2006;118:S197-S202.
- ◆ Stevens B, Yamada J, Ohlsson A: Sucrose for analgesia in newborn infants undergoing painful procedures (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004, Oxford Update Software.
- ◆ Anand KJS and the International Evidence-Based Group for Neonatal Pain: Consensus statement for the prevention and management of pain in the newborn. *Arch Pediatr Adolesc Med* 2001;155:173-180.
- ◆ Gibbons S, Stevens B: Mechanisms of sucrose and non-nutritive sucking in procedural pain management in infants. *Pain Res Manage* 2001;6:21-28.
- ◆ Abad F, Diaz-Gomez NM, Domenech E, et al: Oral sucrose compares favorably with lidocaine-prilocaine cream for pain relief during venepuncture in neonates. *Acta Paediatr* 2001;90:160-165.
- ◆ Blass EM, Watt LB: Suckling and sucrose-induced analgesia in human newborns. *Pain* 1999;83:611-623.
- ◆ Stevens B, Taddio A, Ohlsson A, Einarson T: The efficacy of sucrose for relieving procedural pain in neonates - a systematic review and meta-analysis. *Acta Paediatr* 1997;86:837-842.
- ◆ Bucher H-U, Moser T, Von Siebenthal K, et al: Sucrose reduces pain reaction to heel lancing in preterm infants: A placebo-controlled, randomized and masked study. *Pediatr Res* 1995;38:332-335.
- ◆ Product Information, Sweetease® website: <http://sweetease.respironics.com/>

Dose & Administration, Pharmacology and References updated 7/2009



**Dose & Administration**

0.1 mg/kg (0.03 to 0.15 mg/kg) IV push, as needed for paralysis. Usual dosing interval is 1 to 2 hours. Adjust dose as needed based on duration of paralysis.

**Uses**

Skeletal muscle relaxation/paralysis in infants requiring mechanical ventilation. Proposed desirable effects are improved oxygenation/ventilation, reduced barotrauma, and reduced fluctuations in cerebral blood flow.

**Monitoring**

Monitor vital signs frequently, blood pressure continuously. Use some form of eye lubrication.

**Adverse Effects/Precautions**

Hypoxemia may occur because of inadequate mechanical ventilation and deterioration in pulmonary mechanics. When used alone, cardiovascular side effects are minimal; however, decreases in heart rate and blood pressure have been observed when used concurrently with narcotics.

**Black Box Warning**

According to the manufacturer's black box warning, vecuronium should be administered by adequately trained individuals familiar with its actions, characteristics, and hazards.

**Pharmacology**

Nondepolarizing muscle-relaxant that competitively antagonizes autonomic cholinergic receptors. Sympathetic stimulation is minimal. Vecuronium is metabolized rapidly in the liver to 3-desacetyl-vecuronium, which is 50% to 70% active, and is excreted renally. Newborns, particularly premature infants, are especially sensitive to vecuronium; this sensitivity diminishes with age. Onset of action is 1 to 2 minutes; duration of effect is prolonged with higher doses and in premature infants. Skeletal relaxation/paralysis is reversed by neostigmine and atropine.

**Factors affecting duration of neuromuscular blockade:**

**Potiation:** Acidosis, hypothermia, neuromuscular disease, hepatic disease, cardiovascular disease, aminoglycosides, hypokalemia, hypermagnesemia, renal failure, and younger age.

**Antagonism:** Alkalosis, epinephrine, and hyperkalemia. Sensation remains intact; analgesia should be used for painful procedures.

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**Special Considerations/Preparation**

Available as powder for injection in 10-mg and 20-mg vials. Reconstitute 10 mg-vial with 10 mL of compatible solution (1 mg/mL). After reconstitution- 24 hrs stability in refrigerator. Single use only, discard unused portion. After dilution, use within 24 hours after admixing.

A 0.4-mg/mL dilution may be made by diluting 1 mL of 1-mg/mL concentration with 1.5 mL of preservative-free normal saline. Dilution is stable for 24 hours in refrigerator.

**Solution Compatibility:** D<sub>5</sub>W, LR, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Alprostadil, aminophylline, amiodarone, cefazolin, cimetidine, dobutamine, dopamine, epinephrine, esmolol, fentanyl, fluconazole, gentamicin, heparin, hydrocortisone succinate, isoproterenol, linezolid, lorazepam, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, propofol, ranitidine, trimethoprim-sulfamethoxazole, and vancomycin.

**Incompatibility:** Diazepam, furosemide, ibuprofen lysine, and micafungin.

**Selected References**

- ◆ Martin LD, Bratton SL, O'Rourke P: Clinical uses and controversies of neuromuscular blocking agents in infants and children. *Crit Care Med* 1999;27:1358-1368.
- ◆ Segredo V, Matthay MA, Sharma ML, et al: Prolonged neuromuscular blockage after long-term administration of vecuronium in two critically ill patients. *Anesthesiology* 1990;72:566.
- ◆ Bhutani VK, Abbasi S, Sivieri EM: Continuous skeletal muscle paralysis: Effect on neonatal pulmonary mechanics. *Pediatrics* 1988;81:419.
- ◆ Gravlee GP, Ramsey FM, Roy RC, et al: Rapid administration of a narcotic and neuromuscular blocker: A hemodynamic comparison of fentanyl, sufentanil, pancuronium, and vecuronium. *Anesth Analg* 1988;67:39.
- ◆ Meretoja OA, Wirtavuori K, Neuvonen PJ: Age-dependence of the dose-response curve of vecuronium in pediatric patients during balanced anesthesia. *Anesth Analg* 1988;67:21.
- ◆ Costarino AT, Polin RA: Neuromuscular relaxants in the neonate. *Clin Perinatol* 1987;14:965.
- ◆ Product Information, Bedford Laboratories, 2007

Incompatibility updated 10/2009

Compatibilities updated 7/2009

Adverse Effects/Precautions updated 1/2009

References updated 3/2002



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## DIURETICS

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**Dose & Administration**

0.005 to 0.1 mg/kg per dose IV slow push, IM, or orally.

**Preterm infants less than 34 weeks gestation in the first 2 months of life:** every 24 hours.

**Afterward:** every 12 hours.

**Preterm infants greater than or equal to 34 weeks gestation in the first month of life:** every 24 hours.

**Afterward:** every 12 hours.

Infants with lung disease and normal renal function should be started on a low dose. Infants with congestive heart failure or abnormal renal function will need a higher dose.

**Uses**

Diuretic used in patients with renal insufficiency, congestive heart failure, or significant edema that is refractory to furosemide.

**Monitoring**

Serum electrolytes and urine output. Assess patients receiving digoxin concurrently for potassium depletion. Follow weight changes.

**Adverse Effects/Precautions**

Water and electrolyte imbalances occur frequently, especially hyponatremia, hypokalemia, and hypochloremic alkalosis. Potentially ototoxic, but less so than furosemide. May displace bilirubin from albumin binding sites when given in high doses or for prolonged periods.

**Black Box Warning**

According to the manufacturer's black box warning, bumetanide is a potent diuretic which, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion.

**Pharmacology**

Bumetanide is a loop diuretic with a similar mechanism of action to furosemide. Inhibits chloride reabsorption in the ascending limb of Henle's loop and inhibits tubular sodium transport, causing major loss of sodium and chloride. Increases urinary losses of potassium, calcium, and bicarbonate. Urine sodium losses are lower with bumetanide than furosemide, but urine calcium losses are higher. Decreases CSF production by weak carbonic anhydrase inhibition. Decreases pulmonary transvascular fluid filtration. Increases renal blood flow and prostaglandin secretion. Highly protein bound (greater than 97%). Data from adults indicate excellent oral bioavailability and significant hepatic metabolism (40%) via the cytochrome CYP pathway. Serum half-life varies from 4 to 19 hours in neonates, determined by gestational age, postnatal age, and disease state.

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**Special Considerations/Preparation**

Supplied as 2-, 4-, and 10-mL vials (0.25-mg/mL solution). Contains 1% (10 mg/mL) benzyl alcohol; pH adjusted to 7.

A 0.125 mg/mL dilution may be made by adding 3 mL of 0.25 mg/mL injectable solution to 3 mL preservative-free normal saline for injection. Refrigerated dilution is stable for 24 hours. Discolors when exposed to light.

There is no oral dosing formulation available for neonates. The intravenous formulation, diluted in sterile water and given orally, has been used successfully in infants with congenital heart disease.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Aztreonam, cefepime, furosemide, lorazepam, milrinone, morphine, piperacillin/tazobactam, and propofol.

**Incompatibility:** Dobutamine and midazolam.

**Selected References**

- ◆ Eades SK, Christensen ML: The clinical pharmacology of loop diuretics in the pediatric patient. *Pediatr Nephrol* 1998;12:603-616.
- ◆ Lopez-Sambas AM, Adams JA, Goldberg RN, Modi MW: The pharmacokinetics of bumetanide in the newborn infant. *Biol Neonate* 1997;72:265-272.
- ◆ Sullivan JE, Witte MK, Yamashita TS, Myers CM, Blumer JL: Dose-ranging evaluation of bumetanide pharmacodynamics in critically ill infants. *Clin Pharmacol Ther* 1996;60:424-434. (2 other related articles by same authors in same issue).
- ◆ Shankaran S, Liang K-C, Ilagan N, Fleischmann L: Mineral excretion following furosemide compared with bumetanide therapy in premature infants. *Pediatr Nephrol* 1995;9:159-62.
- ◆ Ward OC, Lam LKT: Bumetanide in heart failure of infancy. *Arch Dis Child* 1977;52:877-882.
- ◆ Product Information, Bedford, 2005.

Compatibilities updated 7/2009

Dose, Pharmacology, Special Considerations, and References updated 1/2009

**Dose & Administration**

**Diuresis:** 10 to 20 mg/kg per dose every 12 hours orally.

**Adjuvant treatment of central diabetes insipidus:** 5 mg/kg per dose every 12 hours orally.

Administer with food (improves absorption).

IV administration not recommended because of a lack of data.

**Note:** Do not confuse with hydrochlorothiazide.

**Uses**

Diuretic used in treating both mild to moderate edema and mild to moderate hypertension. Effects increased when used in combination with furosemide or spironolactone. May improve pulmonary function in patients with BPD. Adjuvant treatment of central diabetes insipidus.

**Monitoring**

Serum electrolytes, calcium, phosphorus, and glucose; urine output and blood pressure.

**Adverse Effects/Precautions**

Hypokalemia and other electrolyte abnormalities. Hyperglycemia. Hyperuricemia. **Do not use in patients with significant impairment of renal or hepatic function.**

**Pharmacology**

Limited data in neonates. Variable absorption from GI tract. Onset of action within 1 hour. Elimination half-life depends on GFR, and is approximately 5 hours. Major diuretic effect results from inhibition of sodium reabsorption in the distal nephron. Increases urinary losses of sodium, potassium, magnesium, chloride, bicarbonate, and phosphorus. Decreases renal excretion of calcium. Inhibits pancreatic release of insulin. Displaces bilirubin from albumin binding sites.

**Special Considerations/Preparation**

Available as a 250 mg/5 mL suspension for oral use.

Injectable formulation available in 500-mg vial as lyophilized powder for reconstitution. Reconstitute 500-mg vial with 18 mL (never less) of sterile water for injection to make a concentration of 28 mg/mL. Use solution immediately after reconstitution; discard unused portion. May further dilute in compatible solution for IV infusion (D<sub>5</sub>W and NS).

**Solution Compatibility:** D5W and NS.

**Terminal Injection Site Compatibility:** Alprostadil.

*continued...*

**Selected References**

- ♦ Dice JE: Physical compatibility of alprostadil with commonly used IV solutions and medications in the neonatal intensive care unit. *J Pediatr Pharmacol Ther* 2006;11:233-236.
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- ♦ Albersheim SG, Solimano AJ, Sharma AK, et al: Randomized, double-blind, controlled trial of long-term diuretic therapy for bronchopulmonary dysplasia. *J Pediatr* 1989;115:615.
- ♦ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 244.
- ♦ Kao LC, Warburton D, Cheng MH, et al: Effect of oral diuretics on pulmonary mechanics in infants with chronic bronchopulmonary dysplasia: Results of a double-blind crossover sequential trial. *Pediatrics* 1984;74:37.
- ♦ Product Information: APP Pharmaceuticals, 2009.
- ♦ Product Information: Merck, 2007.
- ♦ Product Information: Mylan Pharmaceuticals, 2006.

Special Considerations, Compatibilities, and References updated 12/2010  
Updated 3/2003



**Dose & Administration**

**Initial dose:** 1 mg/kg IV slow push, IM, or orally.

May increase to a maximum of 2 mg/kg per dose IV or 6 mg/kg per dose orally.

**Initial intervals:**

**Premature infant:** every 24 hours.

**Fullterm infant:** every 12 hours.

**Fullterm infant older than 1 month:** every 6 to 8 hours.

Consider alternate-day therapy for long-term use.

**Uses**

Diuretic that may also improve pulmonary function.

**Monitoring**

Monitor serum and urine electrolytes and renal function periodically during therapy. Consider performing renal ultrasonography in premature infants as furosemide may precipitate nephrocalcinosis/nephrolithiasis. Follow serum potassium levels closely at initiation, in patients receiving concomitant diuretics or digoxin, and during long-term therapy. Monitor urine output and weight changes. Monitor for signs/symptoms of fluid/electrolyte imbalance.

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, furosemide is a potent diuretic which, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion.

Contraindicated in patients with anuria. Furosemide therapy may lead to increased hyponatremia and a significant rise in serum creatinine in patients receiving indomethacin for PDA closure. Ototoxicity (tinnitus and reversible or irreversible hearing impairment) has been reported, especially with rapid injection, severe renal impairment, higher than recommended doses, hypoproteinemia, or concomitant therapy with aminoglycosides, ethacrynic acid, or other ototoxic drugs. Controlled intravenous infusion is recommended for high-dose parenteral therapy. Avoid concomitant use of aminoglycosides (except in life-threatening cases) and ethacrynic acid. Water and electrolyte imbalances occur frequently, especially hypokalemia, hyponatremia, and hypochloremic alkalosis. Risk for hypokalemia increased with brisk diuresis, inadequate oral intake, presence of cirrhosis, concomitant therapy with corticosteroids, ACTH, or prolonged use of laxatives. Acute urinary retention may occur in patients with symptoms of underlying urinary retention; careful monitoring recommended. In patients at high risk for radiocontrast nephropathy, a higher risk of deterioration of renal function may occur with furosemide therapy. Nephrocalcinosis and nephrolithiasis may occur due to high urinary calcium excretion. This has been reported mainly in premature infants, but cases have occurred in infants with no history of prematurity; monitoring recommended. Hypercalciuria and development of bone demineralization and renal calculi occur with long-term therapy. May displace bilirubin from albumin binding sites when given in high doses or for prolonged periods. Cholestatic jaundice and cholelithiasis have also been reported with loop diuretics (mainly in preterm infants receiving long-term TPN and furosemide therapy. Other adverse events include hypotension, fatigue, nausea, and muscle cramps.

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**Pharmacology**

The diuretic actions of furosemide are primarily at the ascending limb of Henle's loop, and are directly related to renal tubular drug concentration. Furosemide causes major urinary losses of sodium, potassium, and chloride. Urinary calcium and magnesium excretion, and urine pH are also increased. Prostaglandin production is stimulated, with increases in renal blood flow and renin secretion. Free water clearance is increased and CSF production is decreased by weak carbonic anhydrase inhibition. Nondiuretic effects include decreased pulmonary transvascular fluid filtration and improved pulmonary function. Protein binding is extensive, but bilirubin displacement is negligible when using normal doses. Oral bioavailability is good. Time to peak effect when given IV is 1 to 3 hours; duration of effect is approximately 6 hours, although half-life may be as long as 67 hours in the most immature neonates.

**Special Considerations/Preparation**

Furosemide oral solution is available in 8-mg/mL and 10-mg/mL concentrations. Protect from light and discard open bottle after 90 days. The injectable solution may also be used for oral administration. Furosemide for injection is available as a 10-mg/mL concentration in 2-, 4-, and 10-mL single use vials.

A 2-mg/mL dilution may be made by adding 2 mL of the 10-mg/mL injectable solution to 8-mL preservative-free normal saline for injection. Dilution should be used within 24 hours. Protect from light and do not refrigerate.

**Solution Compatibility:** NS, D<sub>5</sub>W, D<sub>10</sub>W, and sterile water for injection.

**Terminal Injection Site Compatibility:** Dex/AA Solutions, fat emulsion. Amikacin, aminophylline, amiodarone, ampicillin, atropine, aztreonam, bumetanide, calcium gluconate, cefepime, ceftazidime, cimetidine, dexamethasone, digoxin, epinephrine, famotidine, fentanyl, heparin, hydrocortisone succinate, ibuprofen lysine, indomethacin, lidocaine, lorazepam, linezolid, meropenem, micafungin, morphine, nitroglycerin, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E<sub>1</sub>, ranitidine, remifentanyl, sodium bicarbonate, sodium nitroprusside, and tobramycin.

**Incompatibility:** Azithromycin, caspofungin, ciprofloxacin, dobutamine, dopamine, erythromycin lactobionate, esmolol, fluconazole, gentamicin, hydralazine, isoproterenol, metoclopramide, midazolam, milrinone, netilmicin, nicardipine, and vecuronium.

*continued...*

## Selected References

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- ◆ Hufnagle KC, Khan SN, Penn D: Renal calcifications: A complication of long-term furosemide therapy in preterm infants. *Pediatrics* 1982;70:360.
- ◆ Ross BS, Pollak A, Oh W: The pharmacological effects of furosemide therapy in the low-birth-weight infant. *J Pediatr* 1978;92:149.
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- ◆ Product Information, Sanofi-Aventis, 2010.
- ◆ Product Information, APP Pharmaceuticals, 2008.

Monitoring, Adverse Effects/Precautions, and References updated 2/2011  
Compatibilities updated 10/2009



**Dose & Administration**

1 to 2 mg/kg per dose every 12 hours orally.

Administer with food (improves absorption).

**Note: Do not confuse with chlorothiazide.**

**Uses**

Diuretic used in treating both mild to moderate edema and mild to moderate hypertension. Effects increased when used in combination with furosemide or spironolactone. May improve pulmonary function in patients with BPD.

**Monitoring**

Serum electrolytes, calcium, phosphorus, and glucose; urine output and blood pressure.

**Adverse Effects/Precautions**

Hypokalemia and other electrolyte abnormalities. Hyperglycemia. Hyperuricemia.

**Do not use in patients with significant impairment of renal or hepatic function.**

**Pharmacology**

Limited data in neonates. Rapidly absorbed from GI tract. Onset of action is within 1 hour. Elimination half-life depends on GFR and is longer than that of chlorothiazide. Major diuretic effect results from inhibition of sodium reabsorption in the distal nephron. Increases urinary losses of sodium, potassium, magnesium, chloride, phosphorus, and bicarbonate. Decreases renal excretion of calcium. Inhibits pancreatic release of insulin. Displaces bilirubin from albumin.

**Special Considerations/Preparation**

Supplied as 12.5 mg capsule and 25, 50, and 100 mg tablets.

Extemporaneous formulation for single ingredient hydrochlorothiazide oral suspension is not available. Below are the extemporaneous compounding instructions for the combination product of spironolactone PLUS hydrochlorothiazide. Spironolactone/hydrochlorothiazide 5 mg/5 mg per mL oral solution can be prepared by using 24 tablets of spironolactone/hydrochlorothiazide 25 mg/25 mg in 120 mL of either a 1:1 mixture of Ora-Sweet(R) and Ora-Plus(R), a 1:1 mixture of Ora-Sweet SF(R) and Ora-Plus(R), or cherry syrup (cherry syrup concentrate diluted 1:4 with simple syrup). Crush tablets to a fine powder, add 25 mL of vehicle, and mix to create a uniform paste. Add vehicle to almost volume, transfer to amber bottle and add vehicle to final volume of 120 mL. Label "shake well" and "protect from light", with expiration date of 60 days. In the stability study, at least 91% of the initial hydrochlorothiazide and spironolactone concentration was retained for up to 60 days when stored without light at 5 and 25 degrees Celcius.

*continued...*

**Selected References**

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- ◆ Albersheim SG, Solimano AJ, Sharma AK, et al: Randomized, double-blind, controlled trial of long-term diuretic therapy for bronchopulmonary dysplasia. *J Pediatr* 1989;115:615.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 244.

Special Considerations/Preparation and References updated 12/2010

**Dose & Administration**

1 to 3 mg/kg per dose every 24 hours orally.

**Uses**

Used in combination with other diuretics in the treatment of congestive heart failure and BPD (situations of increased aldosterone secretion).

**Monitoring**

Follow serum potassium closely during long-term therapy. Also, measuring urinary potassium is a useful indicator of effectiveness.

**Adverse Effects/Precautions**

Rashes, vomiting, diarrhea, paresthesias. Dose-dependent androgenic effects in females. Gynecomastia in males. Headaches, nausea, and drowsiness. Use with caution in patients with impaired renal function. May cause false positive ELISA screening tests for congenital adrenal hyperplasia.

**Black Box Warning**

According to the manufacturer's black box warning, spironolactone has been shown to be a tumorigen in chronic animal toxicity studies.

**Pharmacology**

Competitive antagonist of mineralocorticoids (eg, aldosterone). Metabolized to canrenone and 7-a-thiomethylspironolactone, active metabolites with extended elimination half-lives. Decreases excretion of potassium. Highly protein bound. Increases excretion of calcium, magnesium, sodium, and chloride (small effect). Serum half-life with long term use is 13 to 24 hours. Addition of spironolactone to thiazide diuretic therapy in patients with BPD may yield little, if any, additional benefit.

**Special Considerations/Preparation**

Available in 25-mg, 50-mg, and 100-mg tablets.

A 2.5- or 5-mg/mL oral suspension can be made by crushing five or ten 25-mg spironolactone tablets, respectively, and suspending the powder in 50 mL of simple syrup. Suspensions are stable for 1 month refrigerated.

To prepare 25 mg/mL oral suspension, grind one hundred twenty (120) 25-mg tablets to a fine powder in a mortar. Add 40 mL of vehicle\* and mix to a uniform paste. Then add the vehicle in geometric portions and mix after each addition. Transfer contents of the mortar to the calibrated bottle and add enough vehicle to bring the total volume to 120 mL. Protect from light. Shake well. Suspension is stable for 60 days refrigerated or at room temperature (at 5 and 25 degrees C).

\*Vehicles: 1:1 mixture of Ora-Sweet® and Oral-Plus®; 1:1 mixture of Ora-Sweet SF® and Oral-Plus®; or cherry syrup (cherry syrup concentrate diluted 1:4 with simple syrup).

*continued...*

### Selected References

- ◆ Allen LV Jr, Erickson MA III: Stability of ketoconazole, metolazone, metronidazole, procainamide hydrochloride, and spironolactone in extemporaneously compounded oral liquids. *Am J Health-Syst Pharm* 1996;53:2073-2078.
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- ◆ Loggie JMH, Kleinman LI, Van Maanen EF: Renal function and diuretic therapy in infants and children. Part II. *J Pediatr* 1975;86:657.
- ◆ Product Information, Sandoz, 2009.

Special Considerations and References updated 12/2010  
 Adverse Effects/Precautions updated 1/2009





## GI DRUGS

**Dose & Administration**

2.5 to 5 mg/kg per dose every 6 to 12 hours orally or IV infusion over 15 to 30 minutes.

**Uses**

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

**Monitoring**

Gastric pH may be measured to assess efficacy. Observe for impaired consciousness and reduced spontaneous movements.

**Adverse Effects/Precautions**

Known adverse effects of cimetidine in adults include mental confusion, seizures, renal dysfunction, hepatic dysfunction, flushing and transpiration, neutropenia, diarrhea, hypothalamic-pituitary-gonadal dysfunction, and muscular pain. Cimetidine has been reported to increase the serum level and potentiate toxicity of other drugs such as aminophylline, carbamazepine, diazepam, lidocaine, morphine, phenytoin, procainamide, propranolol, quinidine, theophylline, and warfarin.

**Contraindicated** in patients receiving cisapride due to precipitation of life-threatening arrhythmias.

**Pharmacology**

Inhibits gastric acid secretion by histamine  $H_2$ -receptor antagonism. Peak inhibition occurs in 15 to 60 minutes after both oral and IV administration. Metabolized in the liver via sulfation and hydroxylation to inactive compounds that are 90% renally eliminated. Half-life in neonates is 1.1 to 3.4 hours, and is prolonged in patients with renal or hepatic insufficiency. The sulfoxide metabolite may accumulate in the CNS and cause toxicity. Antacids interfere with absorption; therefore concomitant administration is not recommended.

**Special Considerations/Preparation**

Available as a 150-mg/mL injectable solution in 2-mL single-use vials and 8-mL multidose vials. A 15-mg/mL dilution may be made by adding 1 mL of 150 mg/mL concentration to 9 mL of preservative-free normal saline. Dilution stable for 48 hours. Manufacturer's oral solution (60 mg/mL) contains 2.8% alcohol. A 2.4 mg/mL oral dilution may be prepared by adding 1 mL (60 mg) of manufacturer's oral solution to 24 mL of sterile water. Stable for 14 days refrigerated. Also available in 200-, 300-, 400-, and 800-mg tablets.

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**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acetazolamide, acyclovir, amikacin, aminophylline, ampicillin, atropine, aztreonam, caffeine citrate, cefotaxime, cefoxitin, ceftazidime, clindamycin, dexamethasone, diazepam, digoxin, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, fentanyl, fluconazole, flumazenil, furosemide, gentamicin, glycopyrrolate, heparin, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meperidine, meropenem, metoclopramide, midazolam, milrinone, morphine, nafcillin, nicardipine, nitroprusside, pancuronium, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E<sub>1</sub>, protamine, remifentanyl, sodium bicarbonate, vancomycin, vecuronium, vitamin K<sub>1</sub>, and zidovudine.

**Incompatibility:** Amphotericin B (Immediate precipitation occurs), cefazolin, cefepime, indomethacin, and pentobarbital.

### Selected References

- ◆ Vandenplas Y, Sacre L: The use of cimetidine in newborns. *Am J Perinatol* 1987;4:131.
- ◆ Lloyd CW, Martin WJ, Taylor BD: The pharmacokinetics of cimetidine and metabolites in a neonate. *Drug Intell Clin Pharm* 1985;19:203.
- ◆ Ziemniak JA, Wynn RJ, Aranda JV, et al: The pharmacokinetics and metabolism of cimetidine in neonates. *Dev Pharmacol Ther* 1984;7:30.
- ◆ Aranda JV, Outerbridge EW, Shentag JJ: Pharmacodynamics and kinetics of cimetidine in a premature newborn. *Am J Dis Child* 1983;137:1207.
- ◆ Product Information, Hospira, 2004

Compatibilities updated 7/2009

Text updated 3/1997

**Dose & Administration**

**IV:** 0.25 to 0.5 mg/kg per dose every 24 hours, IV slow push;

Continuous infusion of the daily dose in adults provides better gastric acid suppression than intermittent dosing.

**Oral:** 0.5 to 1 mg/kg per dose every 24 hours orally.

**Uses**

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

**Monitoring**

Gastric pH may be measured to assess efficacy (greater than 4).

**Adverse Effects/Precautions**

The use of H<sub>2</sub> blockers in preterm infants has been associated with an increased risk for late-onset bacterial and fungal sepsis. Routine gastric acid suppression in neonates should be avoided. No short term adverse effects have been reported in infants and children, although data are limited to a few small studies. The most common (less than 5% of patients) adverse effects noted in adults were headache, dizziness, constipation, and diarrhea.

**Pharmacology**

Inhibits gastric acid secretion by histamine H<sub>2</sub>-receptor antagonism. Elimination half-life is dependent on renal function, and decreases with age from 11 hours (range 5 to 22) in neonates to 8 hours (range 4 to 12) by 3 months of age. Oral bioavailability is 42 to 50%.

**Special Considerations/Preparation**

Available as 10-mg/mL solution for intravenous use in 2-mL preservative-free single-dose vials, and 4-mL multidose vials containing 0.9% (9 mg/mL) benzyl alcohol as a preservative. A 1-mg/mL dilution may be made by adding 1 mL of the 10 mg/mL concentrated solution to 9 mL of sterile water for injection. Dilution stable for 7 days at room temperature. Although diluted Pepcid® Injection has been shown to be physically and chemically stable for 7 days at room temperature, there are no data on the maintenance of sterility after dilution. Therefore, it is recommended that if not used immediately after preparation, diluted solutions of Pepcid® Injection should be refrigerated and used within 48 hours.

Pepcid® for oral suspension is supplied as a powder containing 400 mg famotidine. Constitute by slowly adding 46 mL Purified Water and shaking vigorously for 5-10 seconds. Final concentration 40 mg/5 mL (8 mg/mL). Stable at room temperature for 30 days. Shake bottle before each use.

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**Dose & Administration**

0.73 to 1.66 mg/kg per dose orally, once a day.

**Uses**

Treatment of reflux esophagitis.

**Monitoring**

Observe for symptomatic improvement within 3 days. Consider intraesophageal pH monitoring to assess for efficacy (pH greater than 4.0). Measure AST and ALT if duration of therapy is greater than 8 weeks.

**Adverse Effects/Precautions**

Hypergastrinemia and mild transaminase elevations are the only Adverse Effects reported in children who received lansoprazole for extended periods of time. Available data are limited to small studies of infants and children.

**Pharmacology**

Lansoprazole inhibits gastric acid secretion by inhibition of hydrogen-potassium ATPase, the enzyme responsible for the final step in the secretion of hydrochloric acid by the gastric parietal cell ("proton pump"). Extensively metabolized in the liver by CYP 2C19 and 3A4. Onset of action is within one hour of administration, maximal effect is at approximately 1.5 hours. Average elimination half-life is 1.5 hours. Inhibition of acid secretion is about 50% of maximum at 24 hours and the duration of action is approximately 72 hours. The absorption of weakly acidic drugs (eg, digoxin, furosemide) is enhanced. The absorption of weakly basic drugs (eg, ketoconazole) is inhibited.

**Special Considerations/Preparation**

Prevacid® is supplied as a delayed-release capsule and a delayed-release orally disintegrating tablet (ODT) containing either 15 mg or 30 mg lansoprazole for oral administration.

The contents of a capsule can be mixed in 40 mL of apple juice and administered by NG tube. Do not use other liquids. The NG tube should be flushed with additional apple juice after administration. Data for successfully supplying patient-specific, partial doses of lansoprazole through pediatric/neonatal feeding tubes are lacking. In one study attempting to provide a partial dose (orally disintegrating tablet formulation) through a feeding tube, a 7.5 mg dose was administered successfully through an 8 French pediatric feeding tube; however, the same dose partially clogged a 6 French pediatric feeding tube (was able to clear with NS flush) and completely clogged a 5 French pediatric feeding tube.

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**Selected References**

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- ◆ Tran A, Rey E, Pons G, Pariente-Khayat A, et al: Pharmacokinetic-pharmacodynamic study of oral lansoprazole in children. *Clin Pharmacol Ther* 2002;71:359-67.
- ◆ Franco M, Salvia C, Terrin G, Spadaro R, et al: Lansoprazole in the treatment of gastro-oesophageal reflux disease in childhood. *Dig Liver Dis* 2000;32:660-6.
- ◆ Product information, TAP Pharmaceuticals, 2007.

Special Considerations/Preparation and References updated 7/2010



**Dose & Administration**

0.033 to 0.1 mg/kg per dose orally or IV slow push every 8 hours.

**Uses**

To facilitate gastric emptying and GI motility. May improve feeding intolerance. Use in GE reflux patients is controversial.

**Monitoring**

Measure gastric residuals. Observe for increased irritability or vomiting.

**Adverse Effects/Precautions****Black Box Warning**

Metoclopramide can cause tardive dyskinesia. The risk increases with duration of treatment and total cumulative dose. Discontinue drug in patients who develop signs or symptoms of tardive dyskinesia. Treatment with metoclopramide for longer than 12 weeks should be avoided except in rare cases where therapeutic benefit outweighs the risk of developing tardive dyskinesia.

Intended for short-term use (several weeks). Dystonic reactions and extrapyramidal symptoms are seen frequently at higher doses and with prolonged use; children are more susceptible than adults.

**Pharmacology**

Derivative of procainamide. Exact mode of action is unknown; however, metoclopramide has both dopamine-receptor blocking activity and peripheral cholinergic effects. Well absorbed from GI tract. Variable first-pass metabolism by liver. Significant fraction excreted unchanged in urine. Lipid-soluble, large volume of distribution. Serum half-life in adults is 4 hours; prolonged in patients with renal failure.

**Special Considerations/Preparation**

Available as a 5-mg/mL injectable solution (osmolality 280 mOsm/kg).

**Protect from light.** A 0.1 mg/mL dilution may be made by adding 0.4 mL of the 5-mg/mL concentration to 19.6 mL of preservative-free NS. Dilution is stable for 24 hours at room temperature.

Oral preparation available in 1-mg/mL concentration. A 0.1 mg/mL oral dilution may be made by adding 1 mL of the 1 mg/mL concentration to 9 mL simple syrup. Stable for 4 weeks at room temperature.

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, aminophylline, atropine, aztreonam, caffeine citrate, cimetidine, ciprofloxacin, clindamycin, dexamethasone, famotidine, fentanyl, fluconazole, heparin, hydrocortisone, lidocaine, linezolid, meropenem, methadone, midazolam, morphine, multivitamins, piperacillin-tazobactam, potassium chloride, potassium phosphate, prostaglandin E<sub>1</sub>, quinupristin-dalfopristin, ranitidine, remifentanyl, and zidovudine.

**Incompatibility:** Ampicillin, calcium gluconate, cefepime, chloramphenicol, erythromycin lactobionate, furosemide, penicillin G, propofol, and sodium bicarbonate.

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**Selected References**

- ◆ Meadow WL, Bui K, Strates E, et al: Metoclopramide promotes enteral feeding in preterm infants with feeding intolerance. *Dev Pharmacol Ther* 1989;13:38.
- ◆ Machida HM, Forbes DA, Gall DG, et al: Metoclopramide in gastroesophageal reflux of infancy. *J Pediatr* 1988;112:483.
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- ◆ Product Information, Baxter, 2009.

Adverse Effects/Precautions and References updated 12/2010  
Compatibilities updated 7/2009

**Dose & Administration**

Oral: 2 to 5 mg/kg per dose every 12 hours orally.

**Uses**

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

**Monitoring**

Gastric pH may be measured to assess efficacy.

**Adverse Effects/Precautions**

The use of H<sub>2</sub> blockers in preterm infants has been associated with an increased risk for late-onset bacterial and fungal sepsis. Routine gastric acid suppression in neonates should be avoided. Limited data on nizatidine in neonatal patients. One case report of thrombocytopenia. No other adverse effects have been reported in infants or children. Elevations in hepatic enzymes and asymptomatic ventricular tachycardia have been reported in adults.

**Pharmacology**

Inhibits gastric acid secretion by histamine H<sub>2</sub>-receptor antagonism. Peak serum concentration occurs 0.5 to 3 hours after oral administration and is not influenced by food. Bioavailability is quite variable. Greater than 90% eliminated in the urine within 12 hours with 60% excreted unchanged. Elimination half-life in neonates is 3 to 7 hours, and is prolonged in preterm infants and patients with renal insufficiency.

**Special Considerations/Preparation**

Axid® alcohol-free oral solution (15 mg/mL) is supplied in 480 mL bottles. Store at room temperature.

**Selected References**

- ◆ Graham PL, Begg MD, Larson E, et al: Risk factors for late onset gram-negative sepsis in low birth weight infants hospitalized in the neonatal intensive care unit. *Pediatr Infect Dis J* 2006;25:113-117.
- ◆ Saiman L, Ludington E, Pfaller M, et al: Risk factors for candidemia in neonatal intensive care unit patients. *Pediatr Infect Dis J* 2000;19:319-324.
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- ◆ Abdel-Rahman SM, Johnson FK, Connor JD, et al: Developmental pharmacokinetics and pharmacodynamics of nizatidine. *JPGN* 2004;38:442-451.
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- ◆ Product information, Braintree Laboratories, Inc., 2005.

Adverse Effects/Precautions and References updated 1/2010

Added 2006



**Dose & Administration**

0.5 to 1.5 mg/kg per dose orally, once a day.

**Uses**

Short-term (less than 8 weeks) treatment of documented reflux esophagitis or duodenal ulcer refractory to conventional therapy.

**Monitoring**

Observe for symptomatic improvement within 3 days. Consider intraesophageal pH monitoring to assess for efficacy (pH greater than 4.0). Measure AST and ALT if duration of therapy is greater than 8 weeks.

**Adverse Effects/Precautions**

Hypergastrinemia and mild transaminase elevations are the only Adverse Effects reported in children who received omeprazole for extended periods of time. Available data are limited to small studies of infants and children.

**Pharmacology**

Omeprazole inhibits gastric acid secretion by inhibition of hydrogen-potassium ATPase, the enzyme responsible for the final step in the secretion of hydrochloric acid by the gastric parietal cell ("proton pump"). Onset of action is within one hour of administration, maximal effect is at approximately 2 hours. Inhibition of acid secretion is about 50% of maximum at 24 hours and the duration of action is approximately 72 hours.

**Special Considerations/Preparation**

Zegerid® (omeprazole/sodium bicarbonate) is supplied as a 20 mg powder for suspension packet. A 2-mg/mL concentration can be prepared by reconstituting up to a total volume of 10 mL with water. The appropriate dose can be administered through a nasogastric or orogastric tube. The suspension should be flushed through the tube with water or normal saline. Studies regarding stability of this product for partial doses have been conducted. A suspension made from six 20-mg packets mixed to a final volume of 60 mL (final concentration, 2 mg/mL) was stable under refrigeration for at least 45 days. In another study, suspensions of 0.6 to 4 mg/mL were stable under refrigeration for up to 28 days; suspensions of 1 to 4 mg/mL were stable at room temperature for 7 days, with a yellow color change.

Prilosec® is supplied as 2.5-mg and 10-mg unit dose packets for delayed-release oral suspension (omeprazole magnesium) and as delayed-release capsules containing 10, 20, or 40-mg omeprazole as enteric-coated granules.

To prepare the delayed-release suspension, empty the 2.5 mg packet into a container containing 5 mL of water (or the 10 mg packet into a container containing 15 mL of water). Stir and leave 2 to 3 minutes to thicken. Stir and administer appropriate patient-specific dose within 30 minutes. For nasogastric or gastric tube administration, add 5 mL of water to a catheter-tipped syringe then add contents of 2.5 mg packet (or add 15 mL of water to syringe for adding 10 mg packet). Shake syringe immediately and leave 2 to 3 minutes to thicken. Shake syringe and inject patient-specific dose through the tube within 30 minutes. Flush tube with an appropriate amount of water.

### Selected References

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- ◆ Alliet P, Raes M, Bruneel E, Gillis P: Omeprazole in infants with cimetidine-resistant peptic esophagitis. *J Pediatr* 1998;132:352-354.
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- ◆ Product Information, AstraZeneca, 2008.

Special Considerations/Preparation updated 7/2010

**Dose & Administration**

**Oral:** 2 mg/kg per dose every 8 hours.

**IV: Term:** 1.5 mg/kg per dose every 8 hours slow push.

**Preterm:** 0.5 mg/kg per dose every 12 hours slow push.

**Continuous IV infusion:** 0.0625 mg/kg per hour; dose range, 0.04 to 0.1 mg/kg per hour.

**Uses**

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

**Monitoring**

Gastric pH may be measured to assess efficacy.

**Adverse Effects/Precautions**

The use of H<sub>2</sub> blockers in preterm infants has been associated with an increased risk for late-onset bacterial and fungal sepsis. Routine gastric acid suppression in neonates should be avoided. One case report of thrombocytopenia. No other short term adverse effects have been reported in infants or children. Elevations in hepatic enzymes, leukopenia, and bradycardia have been reported in adults.

**Pharmacology**

Inhibits gastric acid secretion by histamine H<sub>2</sub>-receptor antagonism. Peak serum concentration occurs 1 to 3 hours after oral administration and is not influenced by food. Bioavailability is quite variable. Hepatic biotransformation predominates after oral absorption, with 30% excreted unchanged in the urine. In contrast, 70% of an IV dose is excreted unchanged in the urine. Elimination half-life in neonates is 3 to 7 hours, and is prolonged in preterm infants and patients with renal or hepatic insufficiency.

**Special Considerations/Preparation**

Available as a 1 mg/mL preservative-free solution for injection in 50 mL single-dose plastic containers, and a 25 mg/mL injectable solution in 2- and 6-mL vials. A 2 mg/mL dilution may be made by adding 0.8 mL of the 25 mg/mL concentration to 9.2 mL preservative-free sterile water or normal saline for injection. Stable for 48 hours at room temperature. May be given orally; absorption is equivalent to that of the oral solution.

Manufacturer's oral solution (15 mg/mL) contains 7.5% alcohol.

Also available as 150- and 300-mg tablets. May prepare oral solution by crushing a 150-mg tablet and dissolving in 30 mL of sterile water to yield a final concentration of 5 mg/mL. Stable for 28 days refrigerated.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, acetazolamide, amikacin, aminophylline, ampicillin, atropine, aztreonam, cefazolin, cefepime, cefoxitin, ceftazidime, chloramphenicol, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, fentanyl, fluconazole, flumazenil, furosemide, gentamicin, glycopyrrolate, heparin, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, midazolam, milrinone, morphine, nicardipine, nitroprusside, pancuronium bromide, penicillin G, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, protamine, remifentanyl, tobramycin, vancomycin, vecuronium, vitamin K<sub>1</sub>, and zidovudine.

**Incompatibility:** Amphotericin B, pentobarbital, and phenobarbital.

### Selected References

- ◆ Graham PL, Begg MD, Larson E, et al: Risk factors for late onset gram-negative sepsis in low birth weight infants hospitalized in the neonatal intensive care unit. *Pediatr Infect Dis J* 2006;25:113-117.
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- ◆ Sutphen JL, Dillard VL: Effect of ranitidine on twenty-four-hour gastric acidity in infants. *J Pediatr* 1989;114:472.
- ◆ Grant SM, Langtry HD, Brogden RN: Ranitidine: An updated review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in peptic ulcer disease and other allied diseases. *Drugs* 1989;37:801.
- ◆ Product Information, GlaxoSmithKline, 2007

Adverse Effects/Precautions and References updated 1/2010

Compatibilities updated 7/2009

Dose & Administration and References updated 1/2009



**Dose & Administration**

10 to 15 mg/kg per dose orally every 12 hours.

**Uses**

Treatment of cholestasis associated with parenteral nutrition, biliary atresia, and cystic fibrosis. Also used to dissolve cholesterol gallstones.

**Monitoring**

Hepatic transaminases and direct bilirubin concentration.

**Adverse Effects/Precautions**

Nausea/vomiting, abdominal pain, constipation, and flatulence.

**Pharmacology**

Ursodiol is a hydrophilic bile acid that decreases both the secretion of cholesterol from the liver and its intestinal absorption. It is well absorbed orally. After conjugation with taurine or glycine, it then enters the enterohepatic circulation where it is excreted into the bile and intestine. It is hydrolyzed back to the unconjugated form or converted to lithocholic acid which is excreted in the feces. Serum half-life is 3 to 4 days in adults. Dissolution of gallstones may take several months. Aluminum-containing antacids bind ursodiol and inhibit absorption.

**Special Considerations/Preparation**

Available in 300-mg capsules. A liquid suspension may be made by opening ten (10) 300-mg capsules into a glass mortar. Mix this powder with 10 mL of glycerin and stir until smooth. Add 60 mL of Ora-Plus® to the mixture and stir. Transfer the contents of the mortar to a glass amber bottle and shake well. Add a small amount of Orange Syrup to the mortar and rinse. Pour the remaining contents into the amber glass bottle, then add enough simple syrup to make the final volume 120 mL, with a final concentration of 25-mg/mL. Shake vigorously. Mixture is stable for 60 days stored at room temperature or refrigerated.

**Selected References**

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References updated 3/2005

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## RESPIRATORY DRUGS

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### Dose & Administration

**Bronchodilation:** 0.1 to 0.5 mg/kg per dose every 2 to 6 hours via nebulizer.

One MDI actuation per dose (approx. 0.1 mg or 100 mcg) every 2 to 6 hours via MDI with spacer device placed in the inspiratory limb of the ventilator circuit. Simulated neonatal lung models suggest greater delivery when using a spacer with the MDI. Use chlorofluorocarbon-free preparations when administering to neonates.

**Oral:** 0.1 to 0.3 mg/kg per dose orally every 6 to 8 hours.

**Treatment of hyperkalemia:** 0.4 mg/kg per dose every 2 hours via nebulizer.

### Uses

Bronchodilator. Treatment of hyperkalemia.

### Monitoring

Assess degree of bronchospasm. Continuous EKG monitoring. **Consider not administering when heart rate is greater than 180 beats per minute.** Serum potassium.

### Adverse Effects/Precautions

Tachycardia, arrhythmias, tremor, hypokalemia, and irritable behavior.

### Pharmacology

Specific  $\beta_2$ -adrenergic agonist. Minimal cardiovascular effects unless used concurrently with aminophylline. Stimulates production of intracellular cyclic AMP, enhancing the binding of intracellular calcium to the cell membrane and endoplasmic reticulum, resulting in bronchodilation. Enhances mucociliary clearance. Drives potassium intracellular. Studies in vitro indicate that approximately 5% of a MDI dose administered using an in-line holding chamber/spacer device, versus less than 1% of a nebulizer dose, is delivered to the lung. Optimal aerosol dose in neonates is uncertain due to differences in aerosol drug delivery techniques. The therapeutic margin appears to be wide.

Well absorbed when administered orally. Onset of action is 30 minutes; duration is 4 to 8 hours. Serum half-life is approximately 6 hours (adults). Time to peak serum concentration is 3 to 4 hours. Tolerance may develop.

### Special Considerations/Preparation

**Oral dosage form:** Syrup, 2 mg/5 mL.

**Inhalation solution:** Available as either 5 mg/mL, 0.83 mg/mL, 0.42 mg/mL, or 0.21 mg/mL.

A 0.1 mg/mL dilution for inhalation may be made by adding 3 mL of 0.83 mg/mL albuterol concentration to 22 mL of preservative-free normal saline. Label for inhalation use only. Stable for 7 days refrigerated.

**MDI:** Available in a pressurized hydrofluoroalkane metered dose inhaler (contains no chlorofluorocarbons (CFC)). Proventil® HFA and Ventolin® HFA 90 mcg albuterol base per actuation.

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**Selected References**

- ◆ Ballard J, Lugo RA, Salyer JW: A survey of albuterol administration practices in intubated patients in the neonatal intensive care unit. *Respir Care* 2002;47:31-38.
- ◆ Singh BS, Sadiq HF, Noguchi A, Keenan WJ: Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. *J Pediatr* 2002;141:16-20.
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- ◆ Product information, Dey, 2007
- ◆ Product Information, GlaxoSmithKline, 2008

Dose & Administration, Special Considerations, and References updated 1/2009

**Dose & Administration**

**Loading dose:** 8 mg/kg IV infusion over 30 minutes, or orally.

**Maintenance:** 1.5 to 3 mg/kg per dose orally, or IV slow push every 8 to 12 hours (start maintenance dose 8 to 12 hours after the loading dose).

In preterm infants, changing from IV aminophylline to oral theophylline requires no dose adjustment.

**Uses**

Treatment of neonatal apnea, including post-extubation, post-anesthesia, and prostaglandin E<sub>1</sub>-induced. Bronchodilator. May improve respiratory function.

**Monitoring**

Monitor heart rate and check blood glucose periodically with reagent strips. Assess for agitation and feeding intolerance.

**Consider withholding next dose if heart rate is greater than 180 beats per minute.**

When indicated by lack of efficacy or clinical signs of toxicity, serum trough concentration should be obtained. Therapeutic ranges are:

1) Apnea of prematurity: 7 to 12 mcg/mL.

2) Bronchospasm: 10 to 20 mcg/mL (older infants with bronchospasm may need these higher levels because of increased protein binding).

**Adverse Effects/Precautions**

GI irritation. Hyperglycemia. CNS irritability and sleeplessness. May be associated with renal calcifications when used concurrently with furosemide and/or dexamethasone.

**Signs of toxicity:** Sinus tachycardia, failure to gain weight, vomiting, jitteriness, hyperreflexia, and seizures.

**Treatment of Serious Theophylline Toxicity:** Activated charcoal, 1 g/kg as a slurry by gavage tube every 2 to 4 hours. Avoid sorbitol-containing preparations: They may cause osmotic diarrhea.

**Pharmacology**

Stimulates central respiratory drive and peripheral chemoreceptor activity. May increase diaphragmatic contractility. Cerebral blood flow is acutely decreased following IV bolus dose. Renal effects include diuresis and increased urinary calcium excretion. Stimulates gastric acid secretion and may cause GE reflux. Cardiac output is increased due to higher sensitivity to catecholamines. Elimination in preterm infants is primarily as unchanged drug, although significant interconversion to caffeine occurs. In the very immature neonate, the serum half-life of theophylline is prolonged (20 to 30 hours). Theophylline metabolism and clearance mature to adult values by 55 weeks postmenstrual age. Aminophylline salt is 78.9% theophylline. Theophylline administered orally is approximately 80% bioavailable; therefore, no dosage adjustment is necessary when changing from IV aminophylline to PO theophylline.

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**Special Considerations/Preparation**

Available as aminophylline for IV use (25 mg/mL) in 10- and 20-mL vials. Dilute 1 mL (25 mg) with 4 mL NS or D<sub>5</sub>W to yield a final concentration of 5 mg/mL. Stable for 4 days refrigerated.

Oral theophylline is available only as an elixer at a concentration of 80 mg/15 mL (5.33 mg/mL) and contains 20% alcohol. Aminophylline oral solution is no longer available.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA (white precipitate forms within 2 hours) solutions. Acyclovir, ampicillin, amikacin, aztreonam, caffeine citrate, calcium gluconate, ceftazidime, chloramphenicol, cimetidine, dexamethasone, dopamine, enalaprilat, erythromycin lactobionate, esmolol, famotidine, fluconazole, flumazenil, furosemide, heparin, hydrocortisone succinate, lidocaine, linezolid, meropenem, metoclopramide, midazolam, morphine, nafcillin, nicardipine, nitroglycerin, pancuronium bromide, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E<sub>1</sub>, ranitidine, remifentanyl, sodium bicarbonate, vancomycin, and vecuronium.

**Incompatibility:** Amiodarone, cefepime, ceftriaxone, ciprofloxacin, clindamycin, dobutamine, epinephrine, hydralazine, insulin, isoproterenol, methylprednisolone, and penicillin G.

**Selected References**

- ♦ Lim DS, Kulik TJ, Kim DW: Aminophylline for the prevention of apnea during prostaglandin E<sub>1</sub> infusion. *Pediatrics* 2003;112:e27-e29.
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- ♦ Product Information, Hospira, 2004

Dose & Administration, Special Considerations and References updated 10/2009

Compatibilities updated 7/2009

Uses and references updated 3/2004

### Dose & Administration

**Loading dose:** 20 to 25 mg/kg of caffeine citrate IV over 30 minutes or orally.

(Equivalent to 10 to 12.5 mg/kg caffeine base).

**Maintenance dose:** 5 to 10 mg/kg per dose of caffeine citrate IV slow push or orally every 24 hours. (Equivalent to 2.5 to 5 mg/kg caffeine base).

Maintenance dose should be started 24 hours after the loading dose.

May consider an additional loading dose and higher maintenance doses if able to monitor serum concentrations.

(Please note that emphasis has changed to caffeine citrate due to commercially available product. This product (Cafcit®) may be administered both intravenously and orally).

### Uses

Treatment of neonatal apnea, including post-extubation and post-anesthesia. (More favorable therapeutic index than aminophylline).

### Monitoring

Baseline caffeine levels are recommended in neonates previously treated with theophylline and neonates born to mothers who consumed caffeine prior to delivery.

If using the suggested doses, measuring serum concentrations is probably not necessary. Monitoring of serum drug concentration should be based on a trough level determined on approximately day 5 of therapy. Therapeutic trough serum concentration is 5 to 25 mcg/mL. Concentrations greater than 40 to 50 mcg/mL are toxic. Assess for agitation. Monitor heart rate; **consider withholding dose if greater than 180 beats per minute.**

### Adverse Effects/Precautions

Adverse effects are usually mild, and include restlessness, vomiting, and functional cardiac symptoms. There has been a suggested association with NEC, but causality has never been proven. Loading doses of 25 mg/kg caffeine (50 mg/kg caffeine citrate) have been reported to decrease cerebral and intestinal blood flow velocity.

### Pharmacology

The pharmacological effects of caffeine are mediated by its antagonism of the actions of adenosine at cell surface receptors. It is rapidly distributed in the brain, with CNS levels approximating plasma levels. Caffeine increases the respiratory center output, chemoreceptor sensitivity to CO<sub>2</sub>, smooth muscle relaxation, and cardiac output. Oxygen consumption may be increased and weight gain may be reduced. Renal effects include diuresis and increased urinary calcium excretion. Orally administered caffeine citrate is rapidly and completely absorbed. There is almost no first-pass metabolism. In neonates, approximately 86% is excreted unchanged in the urine, with the remainder metabolized via the CYP1A2 enzyme system. The serum half-life of caffeine ranges from 40 to 230 hours, decreasing with advancing postmenstrual age until 60 weeks PMA. Half-life is prolonged in infants with cholestatic hepatitis.

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### Special Considerations/Preparation

Both Cafcit® Oral Solution and Cafcit® Injection for intravenous administration are preservative free and available in 3-mL single use vials. Each mL of Cafcit® contains 20 mg of caffeine citrate (equivalent to 10 mg caffeine base). Store at room temperature.

Alternatively, an oral solution may be prepared by dissolving 2.5 g of caffeine anhydrous powder in 250 mL of water, yielding a final concentration of 10 mg/mL. Solution is stable for 4 weeks refrigerated. Crystals form when stored at low temperature but dissolve at room temperature without loss of potency. **Do not freeze.**

**Solution Compatibility:** D<sub>5</sub>W and D<sub>50</sub>W.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Alprostadil, amikacin, aminophylline, calcium gluconate, cefotaxime, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, doxapram, epinephrine, fentanyl, gentamicin, heparin (concentration less than or equal to 1 unit/mL), isoproterenol, lidocaine, metoclopramide, morphine, nitroprusside, pancuronium, penicillin G, phenobarbital, sodium bicarbonate, and vancomycin.

**Incompatibility:** Acyclovir, furosemide, ibuprofen lysine, lorazepam, nitroglycerin, and oxacillin.

### Selected References

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- ◆ Schmidt B, Roberts RS, Davis P, et al: Caffeine therapy for apnea of prematurity. *N Engl J Med* 2006;354:2112-2121.
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- ◆ Product Information, Bedford Laboratories, 2008

Monitoring and Incompatibility updated 10/2009

Compatibilities updated 7/2009

Dose, Monitoring and References updated 3/2008



**Dose & Administration**

**DART trial protocol:** 0.075 mg/kg per dose every 12 hours for 3 days, 0.05 mg/kg per dose every 12 hours for 3 days, 0.025 mg/kg per dose every 12 hours for 2 days, and 0.01 mg/kg per dose every 12 hours for 2 days.

Doses may be administered IV slow push or orally.

**Uses**

Anti-inflammatory glucocorticoid used to facilitate extubation and improve lung function in infants at high risk for developing chronic lung disease.

**Monitoring**

Assess for hyperglycemia and hyperlipidemia. Monitor blood pressure. Guaiac gastric aspirates. Echocardiogram if treating longer than 7 days.

**Adverse Effects/Precautions**

The February 2002 AAP and CPS statement strongly discourages routine use of dexamethasone. If dexamethasone is used for CLD risk reduction, 1) Treat only those infants at highest risk; 2) Use lower than traditional pharmacologic doses; 3) Begin treatment after Day 7 but before Day 14 of life; 4) Do not give concurrently with indomethacin; 5) Use preservative-free drug wherever possible.

The DART trial found no association with long-term morbidity, but other studies have reported an increased risk of cerebral palsy. Most evidence suggests no increase in the incidence of ROP or the need for cryotherapy. Gastrointestinal perforation and GI hemorrhage occur more frequently in patients treated beginning on Day 1 and in those also being treated concurrently with indomethacin. Hyperglycemia and glycosuria occur frequently after the first few doses, and one case of diabetic ketoacidosis has been reported. Blood pressure increases are common, and hypertension occurs occasionally. Cardiac effects noted by Day 14 of therapy include increased left ventricular wall thickness with outflow tract obstruction and transient impairment of left ventricular filling, systolic anterior motion of the mitral valve, and ST-segment depression. Other potential short-term adverse effects include sodium and water retention, hypokalemia, hypocalcemia, hypertriglyceridemia, increased risk of sepsis, renal stones (in patients receiving furosemide), osteopenia, and inhibition of growth. Adrenal insufficiency may occur secondary to pituitary suppression.

*continued...*

**Pharmacology**

Stabilizes lysosomal and cell membranes, inhibits complement-induced granulocyte aggregation, improves integrity of alveolar-capillary barrier, inhibits prostaglandin and leukotriene production, rightward shifts oxygen-hemoglobin dissociation curve, increases surfactant production, decreases pulmonary edema, relaxes bronchospasm. Hyperglycemia is caused by inhibition of glucose uptake into cells and decreased glucokinase activity. Increased triglyceride synthesis is due to hyperinsulinemia and increased acetyl-CoA carboxylase activity. Blood pressure is increased due to increased responsiveness to endogenous catecholamines. Increases protein catabolism with potential loss of muscle tissue, increases urinary calcium excretion because of bone resorption, and suppresses pituitary ACTH secretion. Biologic half-life is 36 to 54 hours.

**Special Considerations/Preparation**

Dexamethasone sodium phosphate for injection is available in concentrations of 4 mg/mL (benzyl alcohol preservative 10 mg/mL) and 10 mg/mL (preservative free or benzyl alcohol preservative 10 mg/mL). A 0.2 mg/mL dilution may be made by adding 1 mL of the 4 mg/mL concentration to 19 mL preservative-free sterile water for injection. Dilution is stable for 24 hours refrigerated and may be used for oral administration.

A 0.5 mg/mL oral suspension can be made by diluting 1 mL of the 4 mg/mL IV solution up to a total volume of 8 mL with a 1:1 mixture of Ora-Sweet® and Ora-Plus®. The oral suspension is physically and chemically stable for up to 91 days with or without refrigeration.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, aminophylline, aztreonam, caffeine citrate, cefepime, cimetidine, famotidine, fentanyl, fluconazole, furosemide, heparin, hydrocortisone succinate, lidocaine, linezolid, lorazepam, meropenem, methadone, metoclopramide, milrinone, morphine, nafcillin, netilmicin, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanyl, sodium bicarbonate, and zidovudine.

**Incompatibility:** Glycopyrrolate, midazolam, and vancomycin.

*continued...*

### Selected References

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### Adverse Effects

- ◆ Stark AR, Carlo W, Tyson JE, et al: Adverse effects of early dexamethasone treatment extremely low birth weight infants. *N Engl J Med* 2001;344:95-101.
- ◆ Stoll BJ, Temprosa MS, Tyson JE, et al: Dexamethasone therapy increases infection in very low birth weight infants. *Pediatrics* 1999;104(5). URL:[http://www.pediatrics.org/cgi/content/full/104\(5\)/e63](http://www.pediatrics.org/cgi/content/full/104(5)/e63).
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- ◆ Bensky AS, Kothadia JM, Covitz, W: Cardiac effects of dexamethasone in very low birth weight infants. *Pediatrics* 1996;97:818.
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- ◆ Ng PC: The effectiveness and side effects of dexamethasone in preterm infants with bronchopulmonary dysplasia. *Arch Dis Child* 1993;68:330.

### Developmental Follow-up

- ◆ Doyle LW, Davis PG, Morley CJ, et al. DART Study Investigators: Outcome at 2 years of age of infants from the DART study: a multicenter, international, randomized, controlled trial of low-dose dexamethasone. *Pediatrics* 2007;119:716-21.
- ◆ O'Shea TM, Kothadia JM, Klinepeter KL, et al: Randomized placebo-controlled trial of a 42-day tapering course of dexamethasone to reduce the duration of ventilator dependency in very low birth weight infants: Outcome of study participants at 1 year adjusted age. *Pediatrics* 1999;104:15-21.
- ◆ Shinwell ES, Karplus M, Reich D, et al: Early postnatal dexamethasone therapy and increased incidence of cerebral palsy. *Arch Dis Child Fetal Neonatal Ed* 2000;83:F177-181.
- ◆ Product Information, Abraxis, 2006.

Compatibilities updated 7/2009

Special Considerations and References updated 3/2009

**Dose & Administration**

1.25 mL to 2.5 mL via nebulizer, or 0.2 mL/kg instilled directly into the endotracheal tube.

Administer once or twice per day.

**Uses**

Treatment of atelectasis, secondary to mucus plugging, that is unresponsive to conventional therapies.

**Monitoring**

Monitor airway patency. Suction the airway as needed.

**Adverse Effects/Precautions**

Desaturation and/or airway obstruction may occur due to rapid mobilization of secretions.

**Pharmacology**

Pulmozyme® is a highly purified solution of recombinant human deoxyribonuclease (rhDNase, an enzyme that selectively cleaves DNA). The protein is produced by genetically engineered Chinese hamster ovary cells. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes. rhDNase hydrolyzes this DNA to decrease the viscoelasticity of the secretions. Clinical improvements in the thickness of secretions and ventilation usually occur within 3 hours of administration.

**Special Considerations/Preparation**

Pulmozyme® is supplied in single-use ampules. Each ampule contains 2.5 mL of a sterile, clear, colorless, aqueous solution containing 1 mg/mL dornase alfa (2.5 mg per ampule), 0.15 mg/mL calcium chloride dihydrate, and 8.77 mg/mL sodium chloride (22 mg per ampule) with no preservative. The nominal pH of the solution is 6.3. The ampules should be stored in their protective foil pouch under refrigeration (2-8° C, 36-46° F) and protected from strong light. Do not use beyond the expiration date on the ampule.

**Selected References**

- ◆ Erdeve O, Uras N, Atasay B, Arsan S: Efficacy and safety of nebulized recombinant human DNase as rescue treatment for persistent atelectasis in newborns: case-series. *Croat Med J* 2007;48:234-239.
- ◆ Riethmueller J, Borth-Bruhns T, Kumpf M, et al: Recombinant human deoxyribonuclease shortens ventilation time in young, mechanically ventilated children. *Pediatr Pulmonol* 2006;41:61-66.
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- ◆ El Hassan NO, Chess PR, Huysman MWA, et al: Rescue use of DNase in critical lung atelectasis and mucus retention in premature neonates. *Pediatrics* 2001;108:468-471.
- ◆ Reiter PD, Townsend SF, Velasquez R: Dornase alfa in premature infants with severe respiratory distress and early bronchopulmonary dysplasia. *J Perinatol* 2000;20:530-534.
- ◆ Product information, Genentech, 2005.

Added 03/2008

**Dose & Administration**

Administer every 6 to 8 hours as a metered dose inhaler (MDI) or nebulized solution.

Doses studied in intubated neonates range from 2 puffs (34 mcg) to 4 puffs (68 mcg) via MDI with spacer device placed in the inspiratory limb of the ventilator circuit, and 75 to 175 mcg via jet nebulizer. Simulated neonatal lung models suggest greater delivery when using a spacer with the MDI. Use chlorofluorocarbon free preparations when administering to neonates.

Optimal dose in neonates has yet to be determined due to differences in aerosol drug delivery techniques, although the therapeutic margin appears to be wide.

**Uses**

Anticholinergic bronchodilator for primary treatment of chronic obstructive pulmonary diseases and adjunctive treatment of acute bronchospasm. Ipratropium is not useful in the treatment of bronchiolitis.

**Monitoring**

Assess degree of bronchospasm.

**Adverse Effects/Precautions**

Temporary blurring of vision, precipitation of narrow-angle glaucoma, or eye pain may occur if solution comes into direct contact with the eyes.

**Pharmacology**

Ipratropium bromide is a quaternary ammonium derivative of atropine. It produces primarily large airway bronchodilation by antagonizing the action of acetylcholine at its receptor site. It is relatively bronchospasm specific when administered by inhalation because of limited absorption through lung tissue. Peak effect occurs 1 to 2 hours after administration. Duration of effect is 4 to 6 hours in children. The combination of ipratropium with a beta-agonist produces more bronchodilation than either drug individually.

**Special Considerations/Preparation**

**Inhalation Solution:** Supplied in 2.5-mL vials, containing ipratropium bromide 0.02% (200 mcg/mL) in a sterile, preservative-free, isotonic saline solution that is pH-adjusted to 3.4 with hydrochloric acid. It may be mixed with albuterol or metaproterenol if used within 1 hour. Compatibility data are not currently available with other drugs. Store at room temperature in foil pouch provided. Protect from light.

**MDI:** Atrovent® HFA is available in a pressurized metered-dose aerosol unit (contains no chlorofluorocarbons (CFC)). Each actuation delivers 21 mcg of ipratropium from the valve and 17 mcg from the mouthpiece.

*continued...*

**Selected References**

- ◆ Fayon M, Tayara N, Germain C et al: Efficacy and tolerance of high-dose ipratropium bromide vs. terbutaline in intubated premature human neonates. *Neonatology* 2007;91:167-173.
- ◆ Lee H, Arnon S, Silverman M: Bronchodilator aerosol administered by metered dose inhaler and spacer in subacute neonatal respiratory distress syndrome. *Arch Dis Child* 1994;70:F218.
- ◆ Consensus Conference in Aerosol Delivery: Aerosol Consensus Statement. *Respir Care* 1991;36:916.
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- ◆ Gross NJ: Ipratropium bromide. *N Engl J Med* 1988;319:486.
- ◆ Product Information, Dey, 2006
- ◆ Product Information, Boehringer-Ingelheim, 2008

Dose & Administration, Special Considerations and References updated 1/2009

Text updated 3/2008

Added 1/1995

### Dose & Administration

Nitric oxide inhalation therapy (iNO) should be used only after mechanical ventilatory support has been optimized, including the use of surfactant. **Begin at 20 ppm.** If within 4 hours PaO<sub>2</sub> increases to at least 60 torr, decrease to 5 ppm. Continue at 5 ppm and wean FiO<sub>2</sub> as tolerated. When FiO<sub>2</sub> is less than 0.6 and ventilatory support has been decreased, wean iNO in 1 ppm increments at approximately 4 hour intervals as tolerated. Discontinue when stable on 1 ppm for 4 hours. The usual length of treatment is less than 4 days. Infants who cannot be weaned off after 4 days should undergo further diagnostic testing for other diseases. Administer via an FDA/EMA approved delivery system designed to accurately deliver NO uninterrupted into the ventilator system in parts-per-million concentrations that are constant throughout the respiratory cycle, while limiting NO<sub>2</sub> production (e.g., INOvent™).

### Uses

Treatment of term and near-term infants (greater than or equal to 34 weeks GA) with hypoxic respiratory failure (Oxygenation Index greater than 25) associated with clinical or echocardiographic evidence of pulmonary hypertension. It is usually not effective in infants with congenital diaphragmatic hernia. Available evidence does not support use in preterm infants less than 34 weeks GA. The use of iNO in this population should be done under the auspices of a research protocol.

### Monitoring

Continuous monitoring of oxygenation, blood pressure and heart rate are mandatory. Measure blood methemoglobin concentration 4 hours after initiation of therapy and at 24 hour intervals thereafter. Monitoring of inspired gas must provide for continuous measurement of both NO and NO<sub>2</sub> concentrations, with a feedback mechanism that cuts off delivery if NO or NO<sub>2</sub> exceed acceptable limits.

### Adverse Effects/Precautions

Do not use in infants dependent on right-to-left cardiac blood flow. Pulmonary edema has been reported in patients with pre-existing left ventricular dysfunction.

Abrupt discontinuation may result in worsening oxygenation and increased pulmonary artery pressures. The risks of methemoglobinemia and elevated NO<sub>2</sub> levels increase significantly at doses greater than 20 ppm. Methemoglobin has very high affinity for oxygen and has a profound effect on oxygen content. Small increases in methemoglobin cause significant decreases in available oxygen content. Normal methemoglobin levels are less than 1%. In most neonatal studies, methemoglobinemia was defined as levels of 5% to 7%. Cyanosis develops at levels of 10%, although the patients generally remain asymptomatic. At methemoglobin levels approaching 30%, patients begin to experience respiratory distress, and cardiac, gastrointestinal, and neurologic symptoms. A methemoglobin level greater than 50% is usually lethal. Avoid concomitant use of acetaminophen, metoclopramide, sulfa drugs, topical anesthetics (EMLA, benzocaine, lidocaine, prilocaine). Congenital deficiencies in the methemoglobin reductase enzyme system occur but are rare. The environmental exposure limit set by the Occupational Safety and Health Administration is 25 ppm for NO and 5 ppm for NO<sub>2</sub>.

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### Pharmacology

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator that decreases extrapulmonary right-to-left shunting. It activates guanylate cyclase by binding to its heme component leading to production of cyclic GMP, with subsequent relaxation of pulmonary vascular smooth muscle. Oxygenation is also improved due to the redirecting of blood from poorly aerated to better aerated distal air spaces. In addition, iNO appears to have both anti-oxidant and anti-inflammatory activities.

### Special Considerations/Preparation

Nitric oxide for inhalation is supplied in medical grade gas cylinders. Store vertically in well-ventilated areas at room temperature. All cylinders should be returned to the supplier for disposal. Hospital personnel should receive specific training in the administration of iNO.

### Selected References

- ◆ Cole FS, Alleyne C, Barks JD, et al: NIH Consensus Development Conference Statement: Inhaled nitric oxide therapy for preterm infants. *Pediatrics* 2011;127:363-369.
- ◆ Donohue PK, Gilmore MM, Cristofalo E, et al: Inhaled nitric oxide in preterm infants: A systematic review. *Pediatrics* 2011;127:e414-e422.
- ◆ Barrington KJ, Finer N: Inhaled nitric oxide for respiratory failure in preterm infants (Review). In: *The Cochrane Library*, Issue 12, 2010.
- ◆ Finer N, Barrington KJ: Nitric oxide for respiratory failure in infants born at term or near term (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2006. Oxford. Update Software.
- ◆ Clark RH, Huckaby JL, Kueser TJ, et al: Low-dose nitric oxide therapy for persistent pulmonary hypertension: 1-year follow-up. *J Perinatol* 2003; 23(4):300-303.
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- ◆ Finer NN, Sun JW, Rich W, et al: Randomized, prospective study of low-dose versus high-dose inhaled nitric oxide in the neonate with hypoxic respiratory failure. *Pediatrics* 2001;108:948-55.
- ◆ Clark RH, Kueser TJ, Walker MW, et al: Low-dose nitric oxide therapy for persistent pulmonary hypertension of the newborn. *N Engl J Med* 2000;342:469-74.
- ◆ Kinsella JP, Abman SH: Clinical approach to inhaled nitric oxide therapy in the newborn with hypoxemia. *J Pediatr* 2000;136:717-26.
- ◆ The Neonatal Inhaled Nitric Oxide Study Group: Inhaled nitric oxide in term and near-term infants: Neurodevelopmental follow-up of the The Neonatal Inhaled Nitric Oxide Study Group (NINOS). *J Pediatr* 2000;136:611-17.
- ◆ Davidson D, Barefield ES, Kattwinkel J, et al: Safety of withdrawing inhaled nitric oxide therapy in persistent pulmonary hypertension of the newborn. *Pediatrics* 1999;104:231-36.
- ◆ The Neonatal Inhaled Nitric Oxide Study Group: Inhaled nitric oxide in full-term and nearly full-term infants with hypoxic respiratory failure. *N Engl J Med* 1997;336:597-604.
- ◆ Product Information, INO Therapeutics, 2009

Uses and References updated 3/2011

Adverse Effects/Precautions updated 10/2009



**Dose & Administration**

See specific products (beractant, calfactant, or poractant alfa) for dosing and administration information.

**Uses**

**Prophylaxis** of infants at high risk for RDS (those less than 29 weeks gestation).

**Rescue** treatment of infants with moderate to severe RDS.

**Treatment of mature infants with respiratory failure** due to meconium aspiration syndrome, pneumonia, or persistent pulmonary hypertension.

**Monitoring**

Assess ET tube patency and position. Oxygen saturation, EKG, and blood pressure should be monitored continuously during dosing. Assess for impairment of gas exchange caused by blockage of the airway. After dosing, frequent assessments of oxygenation and ventilation should be performed to prevent postdose hyperoxia, hypocarbia, and overventilation.

**Adverse Effects/Precautions**

Administration of exogenous surfactants should be restricted to highly supervised clinical settings, with immediate availability of clinicians experienced with intubation, ventilator management, and general care of premature infants. Reflux of exogenous surfactant up the ET tube and falls in oxygenation occur frequently. If the infant becomes dusky or agitated, heart rate slows, oxygen saturation falls more than 15%, or surfactant backs up in the ET tube, dosing should be slowed or halted. If necessary, ventilator settings and/or  $\text{FiO}_2$  should be turned up. Pulmonary hemorrhage occurs in 2% to 4% of treated infants, primarily the smallest patients with untreated PDA. This may be due to hemorrhagic pulmonary edema caused by the rapid fall in pulmonary vascular resistance and resulting increased pulmonary blood flow.

**Pharmacology**

In infants with RDS, exogenous surfactant therapy reverses atelectasis and increases FRC, with rapid improvements in oxygenation. All preparations reduce mortality from RDS. Natural surfactants are more effective than synthetics in reducing pulmonary air leak. There are no significant differences between preparations in chronic lung disease or other long term outcomes. All commercially available preparations contain surfactant apoprotein C (SP-C), none contain SP-A. The lung-mince extracts Survanta® and Curosurf® contain less than 10% of the SP-B contained in the lung-wash extract Infasurf®.

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**Selected References**♦ **Review Articles**

- ♦ Engle WA and the Committee on Fetus and Newborn: Surfactant-replacement therapy for respiratory distress in the preterm and term neonate. *Pediatrics* 2008;121:419-432.
- ♦ Suresh GK, Soll RF: Current surfactant use in premature infants. *Clin Perinatol* 2001;28:671-694.
- ♦ Rodriguez RJ, Martin RJ: Exogenous surfactant therapy in newborns. *Resp Care Clin North Am* 1999;5:595-616.
- ♦ Kattwinkel J: Surfactant: Evolving issues. *Clin Perinatol* 1998; 25:17-32.
- ♦ Morley CJ: Systematic review of prophylactic vs rescue surfactant. *Arch Dis Child* 1997;77:F70-F74.
- ♦ Halliday HL: Natural vs synthetic surfactants in neonatal respiratory distress syndrome. *Drugs* 1996;51:226-237.

♦ **Selected References for Non-RDS Indications**

- ♦ Lotze A, Mitchell BR, Bulas DI, et al: Multicenter study of surfactant (Beractant) use in the treatment of term infants with severe respiratory failure. *J Pediatr* 1998;132:40.
- ♦ Findlay RD, Taeusch HW, Walther FJ: Surfactant replacement therapy for meconium aspiration syndrome. *Pediatrics* 1996;97:48.

References updated 1/2009

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**(Poractant alfa) Intratracheal Suspension**

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**Dose & Administration**

Initial dose is 2.5 mL/kg per dose intratracheally, divided into 2 aliquots followed by up to two subsequent doses of 1.25 mL/kg per dose administered at 12-hour intervals if needed.

Clear the trachea of secretions. Shorten a 5F end-hole catheter so the tip of the catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle. **Do not filter or shake.**

Attach shortened catheter to syringe. Fill catheter with surfactant. Discard excess through catheter so only total dose to be given remains in syringe.

Administer in two to four aliquots with the infant in different positions to enhance distribution in the lungs. The catheter can be inserted into the infant's endotracheal tube without interrupting ventilation by passing the catheter through a neonatal suction valve attached to the endotracheal tube.

Alternatively, surfactant can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each aliquot, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

**Pharmacology**

Pulmonary lung surfactants are essential for effective ventilation by modifying alveolar surface tension thereby stabilizing the alveoli. Curosurf® is a modified porcine-derived minced lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C. Each mL of surfactant contains 80 mg of total phospholipids (54 mg of phosphatidylcholine of which 30.5 mg dipalmitoyl phosphatidylcholine) and 1 mg of protein including 0.3 mg of SP-B.

**Special Considerations/Preparation**

Available in 1.5 mL (120 mg phospholipid) and 3 mL (240 mg phospholipid) vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Curosurf® for discoloration; normal color is creamy white. If settling occurs during storage, gently turn vial upside-down in order to uniformly suspend. **Do not shake.** Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

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### Selected References

- ◆ Collaborative European Multicenter Study Group: Surfactant replacement therapy for severe neonatal respiratory distress syndrome: A international randomized clinical trial. *Pediatrics* 1988;82:683-691.
- ◆ Bevilacqua G, Parmigiani S, Robertson B: Prophylaxis of respiratory distress syndrome by treatment with modified porcine surfactant at birth: a multicentre prospective randomized trial. *J Perinat Med* 1996;24:609-620.
- ◆ Egberts J, de Winter JP, Sedin G, et al: Comparison of prophylaxis and rescue treatment with Curosurf® in neonates less than 30 weeks' gestation: A randomized trial. *Pediatrics* 1993;92:768-774.
- ◆ Halliday HL, Tarnow-Mordi WO, Corcoran JD, et al: Multicentre randomised trial comparing high and low dose surfactant regimens for the treatment of respiratory distress syndrome (the Curosurf® 4 trials). *Arch Dis Child* 1993;69:276-280.
- ◆ Product Information, Cornerstone Therapeutics, 2010.

Added 3/2000

## (Calfactant) Intratracheal Suspension

## Dose &amp; Administration

Initial dose is 3 mL/kg per dose intratracheally, divided into 2 aliquots followed by up to three subsequent doses of 3 mL/kg per dose administered at 12-hour intervals if needed.

Clear the trachea of secretions. Shorten a 5F end-hole catheter so the tip of the catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle. Do not filter or shake.

Attach shortened catheter to syringe. Fill catheter with surfactant. Discard excess through catheter so only total dose to be given remains in syringe.

Administer in two to four aliquots with the infant in different positions to enhance distribution in the lungs. The catheter can be inserted into the infant's endotracheal tube without interrupting ventilation by passing the catheter through a neonatal suction valve attached to the endotracheal tube.

Alternatively, surfactant can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each aliquot, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

## Pharmacology

Pulmonary lung surfactants are essential for effective ventilation by modifying alveolar surface tension thereby stabilizing the alveoli. Infasurf® is a sterile, non-pyrogenic natural surfactant extracted from calf lungs containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C. Preservative free. Each mL of Infasurf® contains 35 mg of total phospholipids (26 mg of phosphatidylcholine of which 16 mg is disaturated phosphatidylcholine) and 0.7 mg of proteins including 0.26 mg of SP-B.

## Special Considerations/Preparation

Available in 3-mL and 6-mL single-use vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Infasurf® for discoloration; normal color is off-white. If settling occurs during storage, gently swirl vial in order to uniformly suspend. **Do not shake.** Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

## Selected References

- ◆ Bloom BT, Kattwinkel J, Hall RT, et al: Comparison of Infasurf® (calf lung surfactant extract) to Survanta (beractant) in the treatment and prevention of respiratory distress syndrome. *Pediatrics* 1997;100:31-38.
- ◆ Hudak ML, Farrell EE, Rosenberg AA, et al: A multicenter randomized, masked comparison trial of natural versus synthetic surfactant for the treatment of respiratory distress syndrome. *J Pediatr* 1996;128:396-406.
- ◆ Kendig JW, Ryan RM, Sinkin RA, et al: Comparison of two strategies for surfactant prophylaxis in very premature infants: A multicenter randomized trial. *Pediatrics* 1998;101:1006-1012.
- ◆ Product Information, ONY, Inc., 2009

Added 3/2000

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(Beractant) Intratracheal Suspension

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**Dose & Administration**

4 mL/kg per dose intratracheally, divided into 4 aliquots.

**Prophylaxis:** First dose is given as soon as possible after birth, with up to three additional doses in the first 48 hours of life, if indicated.

**Rescue treatment of RDS:** Up to four doses in first 48 hours of life, no more frequently than every 6 hours.

Before administration, allow to stand at room temperature for 20 minutes, or warm in the hand for at least 8 minutes. **Artificial warming methods should not be used.**

Shorten a 5F end-hole catheter so tip of catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle.

Do not filter or shake. Attach shortened catheter to syringe. Fill catheter with Survanta. Discard excess Survanta through catheter so only total dose to be given remains in syringe.

Administer four quarter-doses with the infant in different positions to enhance distribution. The catheter can be inserted into the infant's endotracheal tube through a neonatal suction valve without interrupting ventilation. Alternatively, Survanta can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each quarter-dose, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

**Pharmacology**

Survanta® is a modified natural bovine lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C, to which colfosceril palmitate (DPPC), palmitic acid, and tripalmitin are added. Resulting drug provides 25 mg/mL phospholipids (including 11 to 15.5 mg/mL DPPC), 0.5 to 1.75 mg/mL triglycerides, 1.4 to 3.5 mg/mL fatty acids, and less than 1 mg/mL protein. Survanta® is suspended in NS and heat sterilized. Animal metabolism studies show that most of a dose becomes lung-associated within hours of administration, and lipids enter endogenous surfactant pathways of reuse and recycling.

**Special Considerations/Preparation**

Available in 4- and 8-mL single-use vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Survanta® for discoloration; normal color is off-white to light-brown. If settling occurs during storage, **swirl** vial gently. **Do not shake.** Vials should be entered only once. Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

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**Selected References**

- ◆ Zola EM, Overbach AM, Gunkel JH, et al: Treatment investigational new drug experience with Survanta (beractant). *Pediatrics* 1993;91:546.
- ◆ Hoekstra RE, Jackson JC, Myers TF, et al: Improved neonatal survival following multiple doses of bovine surfactant in very premature neonates at risk for respiratory distress syndrome. *Pediatrics* 1991;88:10.
- ◆ Liechty EA, Donovan E, Purohit D, et al: Reduction of neonatal mortality after multiple doses of bovine surfactant in low birth weight neonates with respiratory distress syndrome. *Pediatrics* 1991;88:19.
- ◆ Product Information, Abbott Laboratories, 2009

Updated 3/2008

RESPIRATORY

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## MISCELLANEOUS DRUGS

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**Dose & Administration**

**Pending definitive diagnosis of urea cycle enzyme deficiency:**

**Loading dose:** Arginine hydrochloride 600 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Arginine hydrochloride 600 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 24 hours.

**Known CPS, OTC, or NAGS deficiency:**

**Loading dose:** Arginine hydrochloride 200 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Arginine hydrochloride 200 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 24 hours.

**Known ASS or ASL deficiency:**

**Loading dose:** Arginine hydrochloride 600 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Arginine hydrochloride 600 mg/kg in combination with sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg as an IV infusion over 24 hours.

**Must be administered through a central line.**

**Dilution:** For loading and maintenance doses, dilute arginine and sodium phenylacetate/sodium benzoate in 25 to 35 mL/kg of D10W prior to administration.

Repeating the loading dose within 24 hours of the initial loading dose should be considered only for patients with a severe disorder receiving dialysis.

CPS = carbamyl phosphate synthetase; OTC = ornithine transcarbamylase; NAGS = N-acetyl glutamate synthase; ASS = argininosuccinic acid synthetase; ASL = argininosuccinic acid lyase

**Uses**

Adjunctive treatment of acute hyperammonemia in neonates with urea cycle disorders. Sodium phenylacetate/sodium benzoate should be used concomitantly with arginine hydrochloride. Hemodialysis is the primary treatment of acute hyperammonemia during the early management period.

**Monitoring**

Plasma ammonia levels every hour during dialysis until levels stabilize to less than 200 to 300 micromoles/L. Capillary blood should not be used for monitoring ammonia levels. Monitor electrolytes and acid-base status closely during the acute phase (eg, every 4 hours). Monitor amino acids daily to assess the effectiveness of citrulline/arginine replacement and glutamine removal.

**Adverse Effects/Precautions**

Hyperchloremic acidosis has been reported. Extravasation can cause tissue necrosis. Arginine is a nitric oxide precursor. Excessive arginine accumulation can result in nitric oxide overproduction with potential for vasodilation and hypotension.

*continued...*

**Pharmacology**

The use of arginine provides an alternative pathway for waste nitrogen excretion in patients with urea cycle disorders, attenuating the risk for ammonia- and glutamine-induced neurotoxicity. Arginine increases the synthesis of citrulline which contains a nitrogen from ammonia and is efficiently excreted in the urine. In addition, certain defects in the urea cycle prevent the formation of citrulline which decreases the synthesis of arginine. This results in arginine becoming an essential amino acid in patients with urea cycle disorders.

**Special Considerations/Preparation**

Arginine hydrochloride is supplied as a 10% solution. The product should be stored at room temperature. Solution that has been frozen should not be used.

**Solution Compatibility:** D<sub>10</sub>W and sodium phenylacetate/sodium benzoate 10%.

**Selected References**

- ◆ Enns GM, Berry SA, Berry GT, et al: Survival after treatment with phenylacetate and benzoate for urea-cycle disorders. *N Engl J Med* 2007;356:2282-2292.
- ◆ The Urea Cycle Disorders Conference Group. Consensus statement from a conference for the management of patients with urea cycle disorders. *J Pediatr* 2001;138:S1-S5.
- ◆ Summar M: Current strategies for the management of neonatal urea cycle disorders. *J Pediatr* 2001;138:S30-S39.
- ◆ Batshaw ML, MacArthur RB, Tuchman M: Alternative pathway therapy for urea cycle disorders: twenty years later. *J Pediatr* 2001;138:S46-S55.
- ◆ Brusilow SW: Arginine, an indispensable amino acid for patients with inborn errors of urea synthesis. *J Clin Invest* 1984;74:2144-2148.
- ◆ Product Information, Pharmacia & Upjohn, 2007

Added 10/2009

**Dose & Administration**

1 or 2 drops instilled in the eye 10 to 30 minutes prior to funduscopy. Use solutions containing concentrations of 0.5% or less in neonates. May be used in conjunction with 1 drop of phenylephrine 2.5% ophthalmic solution.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

**Uses**

Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.

**Monitoring**

Monitor heart rate and assess for signs of ileus prior to feeding.

**Adverse Effects/Precautions**

Feedings should be withheld for 4 hours following procedure. Systemic effects are those of anticholinergic drugs: Fever, tachycardia, vasodilatation, dry mouth, restlessness, delayed gastric emptying and decreased gastrointestinal motility, and urinary retention. The use of solutions with concentrations of 1% or greater have caused systemic toxicity in infants.

**Pharmacology**

Anticholinergic drug that produces pupillary dilation by inhibiting the sphincter pupillae muscle, and paralysis of accommodation. Maximal mydriasis occurs 30 to 60 minutes following administration. Recovery of accommodation occurs in 6 to 24 hours. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

**Special Considerations/Preparation**

Supplied as ophthalmic solution 0.5% in 15-mL Drop-tainers, and 1% and 2% concentrations in 2-, 5- and 15-mL Drop-tainers. Store away from heat. **Do not refrigerate.** A preparation containing cyclopentolate 0.2% and phenylephrine 1% (Cyclomydril®) is commercially available in 2- and 5-mL Drop-tainers.

A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%.

**Selected References**

- ◆ Bonthala S, Sparks JW, Musgrove KH, Berseth CL: Mydriatics slow gastric emptying in preterm infants. *J Pediatr* 2000;137:327-30.
- ◆ Wallace DK, Steinkuller PG: Ocular medications in children. *Clin Pediatr* 1998;37:645.
- ◆ Laws DE, Morton C, Weindling M, Clark D: Systemic effects of screening for retinopathy of prematurity. *Br J Ophthalmol* 1996;80:425-428.
- ◆ McGregor MLK: Anticholinergic agents, in Mauger TF, Craig EL (eds): *Havener's Ocular Pharmacology*, ed 6. St. Louis: Mosby-YearBook, 1994, pp 148-155.
- ◆ Caputo AR, Schnitzer RE, Lindquist TD, Sun S: Dilation in neonates: a protocol. *Pediatrics* 1982;69:77-80.
- ◆ Isenberg S, Everett S: Cardiovascular effects of mydriatics in low-birth-weight infants. *J Pediatr* 1984;105:111-112.
- ◆ Product Information, Falcon, 2004

References updated 3/2001

**Dose & Administration****Hypoglycemia**

**Initial dose:** 0.2 to 1 g/kg IV/IO as D<sub>10</sub>W (2 to 10 mL/kg).

**Maintenance dose:** Continuous infusion of a 5% to 10% dextrose IV solution with appropriate maintenance electrolytes at an initial glucose rate of 6 to 8 mg/kg/minute. Titrate rate to attain normoglycemia. Higher doses may be necessary (10 to 20 mg/kg/minute) to maintain acceptable blood glucose levels, particularly in patients with persistent hyperinsulinemic hypoglycemia.

**Hyperkalemia**

**Initial:** Continuous IV infusion of 0.5 g/kg/hour dextrose and 0.1 to 0.2 units/kg/hour regular insulin. Dextrose and insulin dosages are adjusted based on serum glucose and potassium concentrations.

**Parenteral Nutrition Recommendations** An initial dextrose infusion rate of 6 to 8 mg/kg/minute, advanced as tolerated to a goal rate of 10 to 12 mg/kg/minute, is recommended in neonates. An initial rate of 4 to 8 mg/kg/minute should be considered in preterm neonates.

**Administration** Generally, glucose concentrations greater than 15% should be administered via a central vein to minimize risk of phlebitis and thrombosis. In one study in term neonates (n=121), peripheral infusion of a 20% glucose solution did not cause a higher rate or severity of phlebitis compared with peripheral infusion of a 15% glucose solution. Bolus doses should be administered only by slow IV injection.

**Uses**

Treatment of hypoglycemia. Treatment of hyperkalemia in combination with insulin. Nutritional supplement in parenteral nutrition solutions.

**Monitoring**

Frequent monitoring of blood glucose is recommended. Monitor sodium and potassium levels closely. Obtain urine glucose and electrolytes periodically during therapy. Monitor acid-base balance and fluid status.

**Adverse Effects/Precautions**

**Contraindicated** when intracranial or intraspinal hemorrhage is present. Concentrated dextrose solutions (ie, 25% and 50%) are hypertonic and may cause phlebitis and thrombosis at injection site. Rapid administration may cause significant hyperglycemia and possible hyperosmolar syndrome.

**Pharmacology**

Dextrose restores blood glucose levels in hypoglycemia and provides a source of carbohydrate calories. Intravenous dextrose provides 3.4 kcal/g. When combined with insulin for the treatment of hyperkalemia, dextrose stimulates the sodium-potassium (Na-K) adenosine triphosphatase pump (ATP) leading to an intracellular shift of potassium.

**Special Considerations/Preparation**

Available as 50% concentrated solution in 50-mL single-dose vials and syringes, and 25% concentrated solution in single-use 10-mL syringes. Also available in various other concentrations in large-volume IV solutions.

*continued...*

**Solution Compatibility:** Most standard IV solutions.

**Terminal Injection Site Compatibility:** Most drugs.

**Incompatibility:** Caspofungin, erythromycin, phenytoin, and procainamide.

### Selected References

- ◆ Ahee P, Crowe AV: The management of hyperkalaemia in the emergency department. *J Accid Emerg Med* 2000;17:188-191.
- ◆ ASPEN Board of Directors and the Clinical Guidelines Task Force: Guidelines for the use of parenteral and enteral nutrition in adult and pediatric patients. *JPEN* 2002;26(1 Suppl):1-138.
- ◆ Ditzemberger GR, Collins SD, Binder N: Continuous insulin intravenous infusion therapy for VLBW infants. *J Perinat Nurs* 1999;13:70-82.
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- ◆ Hay WE Jr: Strategies for feeding the preterm infant. *Neonatology* 2008;94:245-254.
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- ◆ Hung KC, Su BH, Lin TW, et al: Glucose-insulin infusion for the early treatment of non-oliguric hyperkalemia in extremely-low-birth-weight infants. *Acta Paediatr Tw* 2001;42:282-286.
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- ◆ Kleinman ME, Chameides L, Schexnayder SM, et al: Part 14: Pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122(suppl 3):S876-S908.
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- ◆ Lehnhardt A, Kemper MJ: Pathogenesis, diagnosis and management of hyperkalemia. *Pediatr Nephrol* 2010;Dec 22 [Epub ahead of print].
- ◆ Lui K, Thungappa U, Nair A, et al: Treatment with hypertonic dextrose and insulin in severe hyperkalaemia of immature infants. *Acta Paediatr* 2002;91:213-216.
- ◆ Malone TA: Glucose and insulin versus cation-exchange resin for the treatment of hyperkalemia in very low birth weight infants. *J Pediatr* 1991;118:121-123.
- ◆ Mildnerberger E, Versmold H: Pathogenesis and therapy of non-oliguric hyperkalaemia of the premature infant. *Eur J Pediatr* 2002;161:415-422.
- ◆ Product Information: 50% Dextrose injection, Hospira, 2004.
- ◆ Product Information: 25% Dextrose injection, Hospira, 2004.
- ◆ Schaefer TJ, Wolford RW: Disorders of potassium. *Emerg Med Clin N Am* 2005;23:723-747.
- ◆ Vanhatalo T, Tammela O: Glucose infusions into peripheral veins in the management of neonatal hypoglycemia - 20% instead of 15%. *Acta Paediatr* 2010;99:350-353.
- ◆ Vemgal P, Ohlsson A: Interventions for non-oliguric hyperkalaemia in preterm neonates. *Cochrane Database of Systematic Reviews* 2007, Issue 1, Art. No.:CCD005257.DOI: 10.1002/14651858.CCD005257.pub 2.

Added 2/2011

**Dose & Administration**

2 to 5 mg/kg per dose orally given every 8 hours. Begin therapy at the higher dosage and taper by response.

**Uses**

Treatment of persistent (more than a few days) or severe hypoglycemia due to hyperinsulinism. Positive responses are usually seen within 48 to 72 hours, and occur in less than 50% of neonates.

**Monitoring**

Periodic CBC and serum uric acid concentrations if treating long term.

**Adverse Effects/Precautions**

Sodium and fluid retention is common—consider concurrent treatment with chlorothiazide (which may also potentiate the hyperglycemic action of diazoxide). There are a few case reports of pulmonary hypertension and cardiac failure, perhaps due to a direct toxic vascular injury. Hyperuricemia, leukopenia, and neutropenia are rare complications. Excessive hair growth and coarse facial features develop with long term use. Ketoacidosis may occur during times of intercurrent illness.

**Pharmacology**

Diazoxide inhibits insulin release by opening ATP-sensitive potassium channels in normal pancreatic beta cells. The opening of these channels also occurs in cardiac and vascular smooth muscle, leading to decreases in blood pressure and the potential for other rare toxic cardiovascular effects. Diazoxide also reduces insulin release and counters the peripheral actions of insulin via catecholamine stimulation. The serum half-life is 10 to 24 hours in infants. Protein binding is more than 90% in adults, and it is primarily excreted unchanged by the kidneys.

**Special Considerations/Preparation**

Proglycem® is available as an oral suspension, 50 mg/mL concentration. Alcohol content is 7.25%. Shake well before use. Protect from light. Store at room temperature.

**Selected References**

- ◆ Nebesio TD, Hoover WC, Caldwell RL, et al: Development of pulmonary hypertension in an infant treated with diazoxide. *J Pediatr Endocrinol Metab* 2007;20:939-44.
- ◆ Hoe FM, Thornton PS, Wanner LA, et al: Clinical features and insulin regulation in infants with a syndrome of prolonged neonatal hyperinsulinism. *J Pediatr* 2006;148:207-212.
- ◆ Schwitzgebel VM, Gitelman SE: Neonatal hyperinsulinism. *Clin Perinatol* 1998;25:1015-1038.
- ◆ Kane C, Lindley KJ, Johnson PRV, et al: Therapy for persistent hyperinsulinemic hypoglycemia of infancy: understanding the responsiveness of beta cells to diazoxide and somatostatin. *J Clin Invest* 1997;100:1888-1893.
- ◆ Stanley CA: Hyperinsulinism in infants and children. *Pediatr Clin North Am* 1997;44:363-374.
- ◆ Product Information, Ivax, 2003

Pharmacology, Adverse Effects, and References updated 3/2008.

### Dose & Administration

Apply 1 to 2 gm to distal half of the penis, then wrap with occlusive dressing. Allow dressing to remain intact for 60 to 90 minutes, remove and clean treated area completely prior to circumcision to avoid systemic absorption.

### Uses

Topical analgesia for circumcision. Not effective for heel lancing.

### Monitoring

Blood methemoglobin concentration if concerned about toxicity.

### Adverse Effects/Precautions

Blanching and redness resolve without treatment. When measured, blood levels of methemoglobin in neonates after the application of 1 g of EMLA cream have been well below toxic levels. Two cases of methemoglobinemia in infants occurred after greater than 3 g of EMLA cream was applied; in 1 of these cases, the infant also was receiving sulfamethoxazole. EMLA cream should not be used in neonates with congenital or idiopathic methemoglobinemia, or who are receiving other drugs known to induce methemoglobinemia: sulfonamides, acetaminophen, nitrates, nitroglycerin, nitroprusside, phenobarbital, and phenytoin.

### Pharmacology

EMLA cream, containing 2.5% lidocaine and 2.5% prilocaine, attenuates the pain response to circumcision when applied 60 to 90 minutes before the procedure. The analgesic effect is limited during the phases associated with extensive tissue trauma such as during lysis of adhesions and tightening of the clamp. Stabilizes the neuronal membranes by inhibiting the ionic fluxes required for conduction and initiation of nerve impulses. There is a theoretic concern about the potential for neonates to develop methemoglobinemia after the application of EMLA cream, because a metabolite of prilocaine can oxidize hemoglobin to methemoglobin. Neonates are deficient in methemoglobin NADH cytochrome b<sub>5</sub> reductase. Lidocaine is metabolized rapidly by the liver to a number of active metabolites and then excreted renally.

### Special Considerations/Preparation

Available in 5-gm and 30-gm tubes with Tegaderm dressing. Each gram of EMLA contains lidocaine 25 mg and prilocaine 25 mg in a eutectic mixture. pH of the product is 9. Contains no preservatives.

### Selected References

- ◆ American Academy of Pediatrics, Task Force on Circumcision. Circumcision policy statement. *Pediatrics* 1999;103:686-693.
- ◆ Taddio A, Ohlsson A, Einarson TR, et al: A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. *Pediatrics* 1998;101:1-9.
- ◆ Lander J, Brady-Fryer B, Metcalfe JB, et al: Comparison of ringblock, dorsal penile nerve block, and topical anesthesia for neonatal circumcision: A randomized controlled trial. *JAMA* 1997;278:2157-2162.
- ◆ Taddio A, Stevens B, Craig K, et al: Efficacy and safety of lidocaine-prilocaine cream for pain during circumcision. *N Engl J Med* 1997;336:1197-1201.
- ◆ Product Information, APP Pharmaceuticals, 2006.

Adverse Effects and References updated 7/2009



**Dose & Administration**

200 mcg/kg per dose (0.2 mg/kg per dose) IV push, IM, or subQ.

**Maximum dose:** 1 mg.

**Continuous infusion:** Begin with 10 to 20 mcg/kg per hour (0.5 to 1 mg per day). Rise in blood glucose should occur within one hour of starting infusion.

**Uses**

Treatment of hypoglycemia refractory to intravenous dextrose infusions, or when dextrose infusion is unavailable, or in cases of documented glucagon deficiency.

**Monitoring**

Follow blood glucose concentration closely. Watch for rebound hypoglycemia. Rise in blood glucose will last approximately 2 hours.

**Adverse Effects/Precautions**

Nausea and vomiting, tachycardia, and ileus. Hyponatremia and thrombocytopenia have also been reported.

**Pharmacology**

Glucagon stimulates synthesis of cyclic AMP, especially in liver and adipose tissue. Stimulates gluconeogenesis. In high doses, glucagon has a cardiac inotropic effect. Inhibits small-bowel motility and gastric-acid secretion.

**Special Considerations/Preparation**

Supplied in 1-mg single-dose vials. Dissolve the lyophilized product in the supplied diluent. Precipitates in chloride solutions. One unit of glucagon and 1 mg of glucagon are equivalent. Use immediately after reconstitution.

**Solution Compatibility:** No data are currently available on Dex/AA and other intravenous solutions.

**Terminal Injection Site Compatibility:** No data are currently available.

**Selected References**

- ◆ Charsha DS, McKinley PS, Whitfield JM: Glucagon infusion for treatment of hypoglycemia: efficacy and safety in sick, preterm neonates. *Pediatrics* 2003;111:220-1.
- ◆ Miralles RE, Lodha A, Perlman M, Moore AM: Experience with intravenous glucagon infusions as a treatment for resistant neonatal hypoglycemia. *Arch Pediatr Adolesc Med* 2002;156:99-1004.
- ◆ Hawdon JM, Aynsley-Green A, Ward Platt MP: Neonatal blood glucose concentrations: metabolic effect of intravenous glucagon and intragastric medium chain triglyceride. *Arch Dis Child* 1993;68:255.
- ◆ Mehta A, Wootton R, Cheng KN, et al: Effect of diazoxide or glucagon on hepatic production rate during extreme neonatal hypoglycemia. *Arch Dis Child* 1987;62:924.
- ◆ Davis SN, Granner DK: Insulin and oral hypoglycemic agents and the pharmacology of the endocrine pancreas, in Hardman JG, Limbird LE, Gilman AG (eds): *The Pharmacological Basis of Therapeutics*, ed 10. New York: Macmillan Co, 2001, pp 1707-08.
- ◆ Product Information, Eli Lilly, 2005

References Updated 3/2004



**Dose & Administration**

Inject 1 mL (150 units) as 5 separate 0.2-mL subcutaneous injections around the periphery of the extravasation site. Use 25- or 26-gauge needle and change after each injection.

The chances of therapeutic success may be increased by:

- 1) Initiating treatment within 1 hour of extravasation;
- 2) Providing small exit stab incisions and subcutaneously flushing the affected area with up to 500 mL of normal saline after the hyaluronidase treatment (technique described by Gault 1993);
- 3) Covering with a hydrogel dressing for 48 hours.

**Uses**

Prevention of tissue injury caused by IV extravasation. Suggested indications (some anecdotal) are for extravasations involving drugs that are irritating to veins because of hyperosmolarity or extreme pH (e.g. aminophylline, amphotericin B, calcium, diazepam, erythromycin, gentamicin, methicillin, nafcillin, oxacillin, phenytoin, potassium chloride, rifampin, sodium bicarbonate, tromethamine, vancomycin, and TPN, and concentrated IV solutions). Hyaluronidase is **not** indicated for treatment of extravasations of vasoconstrictive agents (e.g. dopamine, epinephrine, and norepinephrine).

**Monitoring**

No specific monitoring required.

**Adverse Effects/Precautions**

**Not recommended for IV use.**

**Pharmacology**

Hyaluronidase is a mucolytic enzyme that disrupts the normal intercellular barrier and allows rapid dispersion of extravasated fluids through tissues.

**Special Considerations/Preparation**

Amphadase® and Hydase™ are purified bovine hyaluronidase, and Hylenex® is a recombinant human hyaluronidase. Amphadase®, Hydase™, and Hylenex® are supplied as 150 USP units/mL in 2 mL glass vials. Store refrigerated. Do not freeze.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Incompatibility:** Epinephrine, heparin, and phenytoin.

*continued...*

**Selected References**

- ♦ Ramasethu J: Prevention and management of extravasation injuries in neonates. *NeoReviews* 2004;5:e491-e497.
- ♦ Lehr VT, Lulic-Botica M, Lindblad WJ, et al: Management of infiltration injury in neonates using duoderm hydroactive gel. *Am J Perinatol* 2004;21:409-414.
- ♦ Casanova D, Bardot J, Magalon G: Emergency treatment of accidental infusion leakage in the newborn: report of 14 cases. *Br J Plast Surg* 2001;54:396-399.
- ♦ Davies J, Gault D, Buchdahl: Preventing the scars of neonatal intensive care. *Arch Dis Child* 1994;70:F50-F51.
- ♦ Gault DT: Extravasation injuries. *Br J Plast Surg* 1993;46:91-96.
- ♦ Raszka WV, Kueser TK, Smith FR, Bass JW: The use of hyaluronidase in the treatment of intravenous extravasation injuries. *J Perinatol* 1990;10:146.
- ♦ Product information, Amphastar Pharmaceuticals, Inc., 2005
- ♦ Product information, Akorn, 2007
- ♦ Product information, Baxter Healthcare, 2008

Dose & Administration and References updated 10/2009

Special Considerations, Compatibilities, and References updated 7/2009

**Dose & Administration**

**Physiologic replacement:** 7 to 9 mg/m<sup>2</sup> per day IV or orally, in 2 or 3 doses.

**Treatment of pressor- and volume-resistant hypotension (Stress doses):** 20 to 30 mg/m<sup>2</sup> per day IV, in 2 or 3 doses, or approximately 1 mg/kg per dose every 8 hours.

**Treatment of chorioamnionitis-exposed ELBW infants to decrease risk of CLD:**

Initial dose: 0.5 mg/kg/dose IV every 12 hours for 12 days, followed by 0.25 mg/kg IV every 12 hours for 3 days.

**Body Surface Area**

Weight (kg)	Surface Area (sq meters)
0.6	0.08
1	0.1
1.4	0.12
2	0.15
3	0.2
4	0.25
BSA(m <sup>2</sup> ) = (0.05 × kg) + 0.05	

**Uses**

Treatment of cortisol deficiency. Treatment of pressor-resistant hypotension. Adjunctive therapy for persistent hypoglycemia. May improve survival and decrease CLD in ELBW infants exposed to chorioamnionitis.

**Monitoring**

Measure blood pressure and blood glucose frequently during acute illness.

**Adverse Effects/Precautions**

Hyperglycemia, hypertension, salt and water retention. There is an increased risk of GI perforations when treating concurrently with indomethacin. There is also an increased risk of disseminated *Candida* infections. Early, low-dose hydrocortisone treatment was not associated with increased cerebral palsy. Treated infants had indicators of improved developmental outcome.

**Pharmacology**

Hydrocortisone is the main adrenal corticosteroid, with primarily glucocorticoid effects. It increases the expression of adrenergic receptors in the vascular wall, thereby enhancing vascular reactivity to other vasoactive substances, such as norepinephrine and angiotensin II. Hypotensive babies who are cortisol deficient (less than 15 mcg/dL) are most likely to respond, and blood pressure will increase within 2 hours of the first dose. Hydrocortisone also stimulates the liver to form glucose from amino acids and glycerol, and stimulates the deposition of glucose as glycogen. Peripheral glucose utilization is diminished, protein breakdown is increased, and lipolysis is activated. The net result is an increase in blood glucose levels. Renal effects include increased calcium excretion. The apparent half-life in premature infants is 9 hours.

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**Special Considerations/Preparation**

Hydrocortisone sodium succinate is available as powder for injection in 2-mL vials containing 100 mg. Reconstitute using preservative-free sterile water for injection to 50 mg/mL (reconstituted solution contains 9 mg/mL benzyl alcohol). Also available in 2-, 4-, and 8-mL vials with a concentration of 125 mg/mL after reconstitution. Dilute with preservative-free normal saline or D5W to a final concentration of 1 mg/mL. Dilution stable for 3 days refrigerated.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Acyclovir, amikacin, aminophylline, amphotericin B, ampicillin, atropine, aztreonam, calcium chloride, calcium gluconate, cefepime, chloramphenicol, clindamycin, dexamethasone, digoxin, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, furosemide, heparin, hydralazine, insulin, isoproterenol, lidocaine, linezolid, lorazepam, magnesium, metoclopramide, metronidazole, morphine, neostigmine, netilmicin, nicardipine, oxacillin, pancuronium, penicillin G, piperacillin, piperacillin-tazobactam, potassium chloride, procainamide, propofol, propranolol, remifentanyl, sodium bicarbonate, vecuronium and vitamin K<sub>1</sub>.

**Incompatibility:** Midazolam, nafcillin, pentobarbital, phenobarbital, and phenytoin.

**Selected References**

- ♦ Watterberg KL, Shafer ML, Mishefske MJ, et al: Growth and neurodevelopmental outcomes after early low-dose hydrocortisone treatment in extremely low birth weight infants. *Pediatrics* 2007;120:40-48.
- ♦ Ng PC, Lee CH, Bnur FL, et al: A double-blind, randomized, controlled study of a "stress dose" of hydrocortisone for rescue treatment of refractory hypotension in preterm infants. *Pediatrics* 2006;117:367-375.
- ♦ Watterberg KL, Gerdes JS, Cole CH, et al: Prophylaxis of early adrenal insufficiency to prevent bronchopulmonary dysplasia: a multicenter trial. *Pediatrics* 2004;114:1649-1657.
- ♦ Fernandez E, Schrader R, Watterberg K: Prevalence of low cortisol values in term and near-term infants with vasopressor-resistant hypotension. *J Perinatol* 2004;25:114-118.
- ♦ Seri I, Tan R, Evans J: Cardiovascular effects of hydrocortisone in preterm infants with pressor-resistant hypotension. *Pediatrics* 2001;107:1070-1074.
- ♦ Botas CM, Kurlat I, Young SM, Sola A: Disseminated candidal infections and intravenous hydrocortisone in preterm infants. *Pediatrics* 1995;95:883.
- ♦ Briars GL, Bailey BJ: Surface area estimation: pocket calculator versus nomogram. *Arch Dis Child* 1994;70:246-247.
- ♦ Product Information, Pharmacia and Upjohn, 2003

Compatibilities updated 7/2009

Text and References updated 3/2008

**Dose & Administration****Hyperglycemia:**

**Continuous IV infusion:** 0.01 to 0.1 unit/kg per hour.

[Only regular insulin for injection may be administered intravenously.] To saturate plastic tubing binding sites, fill IV tubing with insulin solution and wait for at least 20 minutes before infusing. The use of higher insulin concentrations and longer wait times will shorten the time to steady-state.

Titrate using blood glucose concentration/reagent strips.

**Intermittent dose:** 0.1 to 0.2 unit/kg every 6 to 12 hours subQ.

**Hyperkalemia:**

**Initial:** Regular insulin 0.1 to 0.2 units/kg/hour in combination with 0.5 g/kg/hour of dextrose given as continuous IV infusion. Insulin and dextrose dosages are adjusted based on serum glucose and potassium concentrations.

**Uses**

Treatment of VLBW hyperglycemic infants with persistent glucose intolerance. Treatment of hyperkalemia in combination with dextrose.

**Monitoring**

Follow blood glucose concentration frequently (every 15 to 30 minutes) after starting insulin infusion and after changes in infusion rate. Monitor potassium concentrations closely when treating hyperkalemia.

**Adverse Effects/Precautions**

May rapidly induce hypoglycemia. Insulin resistance may develop, causing a larger dose requirement. Euglycemic hyperinsulinemia due to exogenous insulin administration may cause metabolic acidosis. The most recent randomized controlled trial (Beardsall) and systematic review (Raney) concluded that routine use of insulin in VLBW infants to promote growth is not warranted.

**Pharmacology**

Degraded in liver and kidney. Enhances cellular uptake of glucose, conversion of glucose to glycogen, amino acid uptake by muscle tissue, synthesis of fat, and cellular uptake of potassium. Inhibits lipolysis and conversion of protein to glucose. Plasma half-life in adults is 9 minutes.

**Special Considerations/Preparation**

Regular human insulin [rDNA origin] is available as 100 units/mL concentration in 10-mL vials. For subcutaneous administration, dilute with sterile water or NS to a concentration of 0.5 or 1 unit/mL. For IV administration, make a 10 units/mL dilution with sterile water, then further dilute in compatible solution to a concentration of 0.05 to 1 unit/mL. **Keep refrigerated.**

**Solution Compatibility:** D<sub>5</sub>W, and D<sub>10</sub>W, and NS.

*continued...*

**Terminal Injection Site Compatibility:** Dex/AA solutions. Amiodarone, ampicillin, aztreonam, caspofungin, cefazolin, cefoxitin, cimetidine, digoxin, dobutamine, esmolol, famotidine, gentamicin, heparin, hydrocortisone succinate, ibuprofen lysine, imipenem, indomethacin, lidocaine, meropenem, midazolam, milrinone, morphine, nitroglycerin, pentobarbital, potassium chloride, propofol, ranitidine, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, tobramycin, and vancomycin.

**Incompatibility:** Aminophylline, dopamine, micafungin, nafcillin, phenobarbital, and phenytoin.

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- ◆ Product Information, Novo Nordisk, 2005

Dose & Administration, Uses, Monitoring, and References updated 2/2011

Compatibilities updated 10/2009

Adverse Effects/Precautions updated 1/2009



**Dose & Administration**

**Initial oral dose:** 10 to 14 mcg/kg per dose orally every 24 hours. (37.5 to 50 mcg/dose for an average term infant).

Dosage is adjusted in 12.5-mcg increments. Always round upward.

**Initial IV dose:** 5 to 8 mcg/kg per dose every 24 hours.

**Uses**

Treatment of hypothyroidism.

**Monitoring**

After 2 weeks of treatment, serum levothyroxine ( $T_4$ ) concentration should be in the high normal range—10 to 16 mcg/dL—and should be maintained in this range for the first year of life. Serum triiodothyronine ( $T_3$ ) concentration should be normal (70 to 220 ng/dL), and TSH should have declined from initial value. After 12 weeks of treatment, serum TSH concentration should be in the normal range, less than 15 mU/L. Serum  $T_4$  and TSH concentrations should be measured at two weeks of age, then every 1 to 2 months, or 2 weeks after any change in dosage. Assess for signs of hypothyroidism: Lethargy, poor feeding, constipation, intermittent cyanosis, and prolonged neonatal jaundice. Assess for signs of thyrotoxicosis: hyperreactivity, altered sleep pattern, tachycardia, tachypnea, fever, exophthalmos, and goiter. Periodically assess growth, development, and bone-age advancement.

**Adverse Effects/Precautions**

Prolonged overtreatment can produce premature craniosynostosis and acceleration of bone age.

**Pharmacology**

Tissue deiodination converts  $T_4$  to  $T_3$ , the active metabolite. Elimination of both  $T_4$  and  $T_3$  is equally in the urine and feces. Clinical effects will persist for 1 week after discontinuation of the drug. Levothyroxine prepared as an oral suspension is 50% to 80% bioavailable. Oral dosing produces effects within 3 to 5 days, while IV dosing produces effects in 6 to 8 hours.

*continued...*

**Special Considerations/Preparation**

Oral suspension is not commercially available. Available as scored tablets ranging from 25 to 300 mcg per tablet. Also available in capsules that contain a viscous liquid ranging from 13 to 150 mcg per capsule. **Capsules cannot be crushed, suspended in water, or dissolved by placing in water before use.** Monitor patient closely when switching brand of drug due to some differences in bioavailability.

To prepare a 15-mcg/mL levothyroxine oral suspension: Crush levothyroxine 100-mcg tablets in glycerol and add sterile water up to desired volume. Shake well before dispensing. Product stability is 10 days when refrigerated between 2 and 8 degrees C. Stability tests demonstrated a 12% decline in levothyroxine concentration in the prepared suspension over 11 days.

An oral liquid formulation of levothyroxine sodium 25 mcg/mL in 40% glycerol compounded from crushed tablets and distilled water with no preservatives added was stable for 8 days when stored in amber bottles at 4 degrees C. Degradation occurred faster in the formulation with preservative (methylparaben).

**The injectable form should not be given orally**, as it crystallizes when exposed to acid. Injectable form is available as lyophilized powder in vials containing 200 or 500 mcg. Use only NS for reconstitution. Manufacturer's suggested final concentrations are 40 mcg/mL or 100 mcg/mL; however, suggested dilution is a final concentration of 20 mcg/mL. **Use immediately. Do not add to any other IV solution.**

**Selected References**

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- ◆ Selva KA, Mandel SH, Rien L, et al: Initial treatment of L-thyroxine in congenital hypothyroidism. *J Pediatr* 2002;141:786-92.
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- ◆ Germak JA, Foley TP: Longitudinal assessment of L-thyroxine therapy for congenital hypothyroidism. *J Pediatr* 1990;117:211.
- ◆ Product Information, Bedford, 2003.

Special Considerations and References updated 12/2010

**Dose & Administration****Treatment of hyperinsulinemic hypoglycemia:**

**Initial dose:** 1 mcg/kg per dose every 6 hours subQ or IV. Titrate upward to desired effect. Initial response should occur within 8 hours; tachyphylaxis may occur within several days.

**Maximum dose:** 10 mcg/kg per dose every 6 hours.

**Treatment of chylothorax:**

Begin at 1 mcg/kg per hour IV continuous infusion. Titrate upward as necessary based on reduction in chyle production; dosage increases of 1 mcg/kg/hour every 24 hours have been used. Infusion is decreased gradually over 2 to 7 days.

**Maximum dose:** 10 mcg/kg/hour.

Has also been used subQ or IV in divided doses.

**Uses**

Treatment of refractory hyperinsulinemic hypoglycemia. Adjunctive treatment of congenital and post-operative chylothorax.

**Monitoring**

Monitor blood glucose closely. Monitor for signs and symptoms of necrotizing enterocolitis.

**Adverse Effects/Precautions**

Vomiting, diarrhea, abdominal distention and steatorrhea may occur. Pulmonary hypertension has been reported in treated former premature infants with chronic lung disease. Necrotizing enterocolitis has been reported in term neonates receiving octreotide for the treatment of hyperinsulinemic hypoglycemia (6 cases) and chylothorax (2 cases). Hyperglycemia may occur in patients being treated for chylothorax.

**Pharmacology**

Octreotide is a long-acting analog of the natural hormone somatostatin. It is an even more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses LH response to GnRH, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide. After subcutaneous injection, octreotide is absorbed rapidly and completely from the injection site. The elimination half-life of octreotide from plasma is approximately 1.7 hours in adults, compared with 1 to 3 minutes for the natural hormone. Excreted unchanged into the urine.

**Special Considerations/Preparation**

Available in 1-mL single-dose ampules for injection containing 50-, 100-, or 500-mcg, and in 5-mL multiple-dose vials in concentrations of 200 and 1000 mcg/mL. pH 3.9 to 4.5. Osmolarity is 279 mOsm/kg. Refrigerate and protect from light. Do not warm artificially. After initial use, multiple dose vials should be discarded within 14 days. Ampuls should be opened just prior to administration and the unused portion discarded. For subQ injection use undiluted drug unless dose volume is not accurately measurable. For continuous IV administration consider making a dilution of 10 to 25 mcg/mL using D<sub>5</sub>W or NS.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W and NS.

**Solution Incompatibility:** Do not add directly to Dex/AA bag because of the formation of glycosyl octreotide conjugate.

**Terminal Injection Site Compatibility:** Dex/AA and heparin.

**Incompatibility:** Micafungin.

### Selected References

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- ◆ Product Information, Novartis, 2005

Dosing & Administration and References updated 2/2011

Monitoring, Adverse Effects and References updated 7/2010

Compatibilities updated 7/2009

**Dose & Administration**

1 drop instilled in the eye at least 10 minutes prior to fundoscopic procedures.

Use **only** the 2.5% ophthalmic solution in neonates.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

**Uses**

Induction of mydriasis for diagnostic and therapeutic ophthalmic procedures.

**Monitoring**

Monitor heart rate and oxygen saturation in babies with BPD.

**Adverse Effects/Precautions**

May cause decreased pulmonary compliance, tidal volume, and peak airflow in babies with BPD. Do not use in patients receiving beta-blocker medications (e.g. propranolol). The use of 10% solutions has caused systemic hypertension and tachycardia in infants.

**Pharmacology**

Alpha-adrenergic. Mydriasis begins within 5 minutes of instillation and lasts for 60 minutes. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

**Special Considerations/Preparation**

Supplied as ophthalmic solution in 0.12%, 2.5%, and 10% concentrations in 2 to 15 mL quantities. Do not use solution that becomes discolored or contains precipitate. Refer to specific product or manufacturer's recommendation for storage.

A preparation containing cyclopentolate 0.2% and phenylephrine 1% (Cyclomydril®) is commercially available in 2- and 8-mL Drop-tainers. A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%.

Use within 24 hours, as the solution contains no preservatives.

*continued...*

**Selected References**

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- ◆ Mirmanesh SJ, Abbasi S, Bhutani VK: Alpha-adrenergic bronchoprovocation in neonates with bronchopulmonary dysplasia. *J Pediatr* 1992;121:622-625.
- ◆ Isenberg S, Everett S: Cardiovascular effects of mydriatics in low-birth-weight infants. *J Pediatr* 1984;105:111-112.
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- ◆ Borromeo-McGrall V, Bordiuk JM, Keitel H: Systemic hypertension following ocular administration of 10% phenylephrine in the neonate. *Pediatrics* 1973;51:1032-1036.
- ◆ Product Information, Alcon, 2005

Added 3/1999

**Dose & Administration****Dosage based on base deficit:**

$\text{HCO}_3^-$  needed (mEq) =  $\text{HCO}_3^-$  deficit (mEq/L)  $\times$  (0.3  $\times$  body wt [kg])

Administer half of calculated dose, then assess need for remainder.

**Usual dosage:** 1 to 2 mEq/kg IV over at least 30 minutes.

**Recommended dilution:** 0.25 mEq/mL.

**Maximum concentration:** 0.5 Eq/mL.

Can also be administered by continuous IV infusion or orally.

**Uses**

Treatment of normal anion gap metabolic acidosis caused by renal or GI losses.

Sodium bicarbonate is not a recommended therapy in neonatal resuscitation guidelines. Administration during brief CPR may be detrimental. Administration during prolonged resuscitation remains controversial - use only after adequate ventilation is established and there is no response to other therapies.

**Monitoring**

Follow ABGs, acid/base status, serum calcium and potassium.

**Adverse Effects/Precautions**

Bicarbonate administered during inadequate ventilation increases  $\text{PCO}_2$ , thereby decreasing pH. Rapid infusion of hypertonic solution is linked to IVH. Local tissue necrosis at IV site. Hypocalcemia, hypokalemia, and hypernatremia.

**Pharmacology**

When bicarbonate is administered, buffering of hydrogen ions occurs, leading to increased production of carbon dioxide and water. Animal studies of resuscitation demonstrate poor coronary perfusion leads to carbon dioxide accumulation within the myocardium, leading to decreased myocardial contractility.

**Special Considerations/Preparation**

Supplied by many manufacturers in multiple concentrations: 4% (0.48 mEq/mL), 4.2% (0.5 mEq/mL; 1 mOsmol/mL), 5% (0.6 mEq/mL; 1.19 mOsmol/mL), 7.5% (0.9 mEq/mL; 1.79 mOsmol/mL) and 8.4% (1 mEq/mL; 2 mOsmol/mL). Maximum concentration used in neonates is 4.2% (0.5 mEq/mL). May dilute with sterile water for injection. Do not infuse with calcium or phosphate containing solutions; precipitation will occur.

*continued...*

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Acyclovir, amikacin, aminophylline, amphotericin B, atropine, aztreonam, cefepime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, erythromycin lactobionate, esmolol, famotidine, furosemide, heparin, hydrocortisone succinate, ibuprofen lysine, indomethacin, insulin, lidocaine, linezolid, milrinone, morphine, nafcillin, netilmicin, penicillin G, phenobarbital, piperacillin-tazobactam, potassium chloride, propofol, remifentanyl, vancomycin, and vitamin K<sub>1</sub>.

**Incompatibility:** Dex/AA. Amiodarone, ampicillin, calcium chloride, cefotaxime, dobutamine, dopamine, epinephrine, glycopyrrolate, imipenem/cilastatin, isoproterenol, magnesium sulfate, meropenem, methadone, metoclopramide, midazolam, nicardipine, norepinephrine, oxacillin, phenytoin, and ticarcillin/clavulanate.

### Selected References

- ◆ Aschner JL, Poland RL: Sodium bicarbonate: basically useless therapy. *Pediatrics* 2008;122:831-835.
- ◆ van Allen-van der Velden AA, Hopman JC, Klaessens JH, et al: Effects of rapid versus slow infusion of sodium bicarbonate on cerebral hemodynamics and oxygenation in preterm infants. *Biol Neonate* 2006;90:122-127.
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- ◆ Howell JH: Sodium bicarbonate in the perinatal setting—revisited. *Clin Perinatol* 1987;14:807.
- ◆ Product Information, Hospira, 2004.

Special Considerations updated 12/2010

Compatibilities updated 10/2009

Dose & Administration, Uses, Monitoring, Adverse Effects/Precautions, Pharmacology, and References updated 1/2009



### Dose & Administration

**Pending definitive diagnosis of urea cycle enzyme deficiency:**

**Loading dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 600 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 600 mg/kg as an IV infusion over 24 hours.

**Known CPS, OTC, or NAGS deficiency:**

**Loading dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 200 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 200 mg/kg as an IV infusion over 24 hours.

**Known ASS or ASL deficiency:**

**Loading dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 600 mg/kg as an IV infusion over 90 to 120 minutes.

**Maintenance dose:** Sodium phenylacetate 250 mg/kg and sodium benzoate 250 mg/kg in combination with arginine hydrochloride 600 mg/kg as an IV infusion over 24 hours.

**Must be administered through a central line.**

**Dilution:** For loading and maintenance doses, dilute sodium phenylacetate/sodium benzoate and arginine in 25 to 35 mL/kg of D<sub>10</sub>W prior to administration.

Repeating the loading dose within 24 hours of the initial loading dose should be considered only for patients with a severe disorder receiving dialysis.

CPS = carbamyl phosphate synthetase; OTC = ornithine transcarbamylase; NAGS = N-acetyl glutamate synthase; ASS = argininosuccinic acid synthetase; ASL = argininosuccinic acid lyase

### Uses

Adjunctive treatment of acute hyperammonemia in neonates with urea cycle disorders. Arginine hydrochloride should be used concomitantly with sodium phenylacetate/sodium benzoate. Hemodialysis is the primary treatment of acute hyperammonemia during the early management period.

### Monitoring

Plasma ammonia levels every hour during dialysis until levels stabilize to less than 200 to 300 micromoles/L. Capillary blood should not be used for monitoring ammonia levels. Monitor electrolytes (especially potassium) and acid-base status closely during the acute phase (eg, every 4 hours). Toxicity due to ammonia scavenging drugs presents as ketoacidosis. An anion gap that is > 15 mEq/L or has risen > 6 mEq/L from baseline may indicate drug accumulation. Monitor amino acids daily to assess the effectiveness of citrulline/arginine replacement and glutamine removal.

*continued...*

**Adverse Effects/Precautions**

Caution advised for use in patients with congestive heart failure, severe renal impairment, or other clinical conditions involving sodium retention with edema; product contains 30.5 mg of sodium per mL. The most common adverse effects include vomiting (9%), hyperglycemia (7%), and hypokalemia (7%). Vomiting and lethargy can occur with higher than recommended doses. Potentially life-threatening toxicity can occur with doses greater than 750 mg/kg per day.

**Pharmacology**

The use of sodium phenylacetate and sodium benzoate provides an alternative pathway for waste nitrogen excretion in patients with urea cycle disorders, attenuating the risk for ammonia- and glutamine-induced neurotoxicity. Phenylacetate is conjugated with glutamine via acetylation to form phenylacetylglutamine. Phenylacetylglutamine is excreted by the kidney and results in removal of 2 moles of waste nitrogen for each mole of phenylacetate administered. Benzoate is conjugated with glycine to form hippurate. Hippurate is excreted by the kidney and results in removal of 1 mole of waste nitrogen for each mole of benzoate administered.

**Special Considerations/Preparation**

Sodium phenylacetate/sodium benzoate (Ammunol®) is available as a 10%/10% solution in a single-use glass vial containing 50 mL. Contains 30.5 mg of sodium per mL.

During the admixture process, the Millex® Durapore GV 33 mm Sterile Syringe Filter (0.22 micrometer) provided by the manufacturer must be used when injecting Ammunol® into the 10% dextrose IV bag.

**Solution Compatibility:** D<sub>10</sub>W and arginine hydrochloride 10%.

**Selected References**

- ◆ Enns GM, Berry SA, Berry GT, et al: Survival after treatment with phenylacetate and benzoate for urea-cycle disorders. *N Engl J Med* 2007;356:2282-2292.
- ◆ The Urea Cycle Disorders Conference Group. Consensus statement from a conference for the management of patients with urea cycle disorders. *J Pediatr* 2001;138:S1-S5.
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- ◆ Batshaw ML, MacArthur RB, Tuchman M: Alternative pathway therapy for urea cycle disorders: twenty years later. *J Pediatr* 2001;138:S46-S55.
- ◆ Product Information, Urcyld Pharma, 2008

Added 10/2009

(Tromethamine)

**Dose & Administration**

1 to 2 mmol/kg (3.3 to 6.6 mL/kg) per dose IV.

Infuse in a large vein over at least 30 minutes.

Dose (of the 0.3 M solution) may be calculated from the following formula:

$$\text{Dose (mL)} = \text{Weight (kg)} \times \text{Base deficit (mEq/L)}$$

Maximum dose in neonates with normal renal function is approximately 5 to 7 mmol/kg per 24 hours. Clinical studies support only short term use.

**Uses**

Treatment of metabolic acidosis, primarily in mechanically ventilated patients with significant hypercarbia or hypernatremia. **Do not use in patients who are anuric or uremic.** THAM is not indicated for treatment of metabolic acidosis caused by bicarbonate deficiency.

**Monitoring**

Observe IV site closely for signs of extravasation. Follow blood-gas results to assess therapeutic efficacy. Follow urine output. Monitor for respiratory depression, hypoglycemia, and hyperkalemia when using several doses.

**Adverse Effects/Precautions**

Most reports of toxicity in neonates (hypoglycemia, hyperkalemia, liver necrosis) were related to rapid umbilical venous infusion of high doses of THAM base solutions that were more alkaline and hypertonic than the THAM acetate solution currently available from Abbott (pH 8.6; osmolality 380 mOsm/L). **Irritating to veins.**

**Pharmacology**

THAM (Tris-Hydroxymethyl Aminomethane) is a proton acceptor that generates  $\text{NH}_3^+$  and  $\text{HCO}_3^-$  without generating  $\text{CO}_2$ . The protonated  $\text{R-NH}_3^+$  is eliminated by the kidneys. Unlike bicarbonate, THAM does not require an open system for  $\text{CO}_2$  elimination in order to exert its buffering effect.

**Special Considerations/Preparation**

Supplied as a 0.3-M solution (1 mmol = 3.3 mL) in a 500-mL single-dose container with no bacteriostatic agent. Intended for single-dose use and unused portion should be discarded.

**Compatibilities:** No data are currently available on solutions and additives.

**Selected References**

- ◆ Holmdahl MH, Wiklund L, Wetterberg T, et al: The place of THAM in the management of acidemia in clinical practice. *Acta Anaesthesiol Scand* 2000;44:524-527.
- ◆ Nahas GG, Sutin KM, Fermon C, et al: Guidelines for the treatment of acidemia with THAM. *Drugs* 1998;55:191-224. (Errata published 1998;55:517).
- ◆ Baum JD, Robertson NRC: Immediate effects of alkaline infusion in infants with respiratory distress syndrome. *J Pediatr* 1975;87:255.
- ◆ Strauss J: Tris (hydroxymethyl amino-methane [THAM]): A pediatric evaluation. *Pediatrics* 1968;41:667.
- ◆ Gupta JM, Dahlenburg GW, Davis JW: Changes in blood gas tensions following administration of amine buffer THAM to infants with respiratory distress syndrome. *Arch Dis Child* 1967;42:416-427.
- ◆ Product Information, Hospira, 2006.

Text and references updated 3/2001

**Dose & Administration**

1 drop instilled in the eye at least 10 minutes prior to funduscopy procedures.

Use **only** the 0.5% ophthalmic solution in neonates.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

**Uses**

Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.

**Monitoring**

Monitor heart rate and assess for signs of ileus prior to feeding.

**Adverse Effects/Precautions**

Feedings should be withheld for 4 hours following procedure. Systemic effects are those of anticholinergic drugs: Fever, tachycardia, vasodilatation, dry mouth, restlessness, decreased gastrointestinal motility, and urinary retention. The use of solutions with concentrations of 1% or greater have caused systemic toxicity in infants.

**Pharmacology**

Anticholinergic drug that produces pupillary dilation by inhibiting the sphincter pupillae muscle, and paralysis of accommodation. Mydriasis begins within 5 minutes of instillation, cycloplegia occurs in 20 to 40 minutes. Recovery of accommodation occurs in 6 hours. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

**Special Considerations/Preparation**

Supplied as ophthalmic solution in 0.5%, and 1% concentrations in 2-, 3-, and 15-mL dropper bottles. Store away from heat. **Do not refrigerate.**

A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%. Use within 24 hours, as the solution contains no preservatives.

**Selected References**

- ◆ Wallace DK, Steinkuller PG: Ocular medications in children. *Clin Pediatr* 1998;37:645-652.
- ◆ Laws DE, Morton C, Weindling M, Clark D: Systemic effects of screening for retinopathy of prematurity. *Br J Ophthalmol* 1996;80:425-428.
- ◆ McGregor MLK: Anticholinergic agents, in Mauger TF, Craig EL (eds): *Havener's Ocular Pharmacology*, ed 6. St. Louis: Mosby-YearBook, 1994, pp 148-155.
- ◆ Caputo AR, Schnitzer RE, Lindquist TD, Sun S: Dilation in neonates: a protocol. *Pediatrics* 1982;69:77-80.
- ◆ Product Information, Alcon, 2004

Added 3/1999



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## VITAMINS/MINERALS

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**Dose & Administration**

Usual dosage: 1 dropperful (1 mL) orally every 24 hours.

Percentages of the Reference Daily Intakes (%RDIs) listed in the table below are for healthy infants 0 to 6 months of age.

**AquADEKs™ Pediatric Liquid**

	Vitamins	% Daily value
-	Amount per mL	0-6 months of age
A (IU)	5751	432
C (mg)	45	113
D3 (IU)	400	200
E (IU)	50	839
E (mg)	15	*
K1 (mcg)	400	20,000
B1 (mg)	0.6	300
B2 (mg)	0.6	200
Niacin (mg)	6	300
B6 (mg)	0.6	600
Biotin (mcg)	15	300
Pantothenic acid (mg)	3	176
Zinc (mg)	5	250
Selenium (mcg)	10	67
Beta-carotene (mg)	3	*
Coenzyme Q (mg)	2	*
*Daily value not established.		

**Uses**

Multivitamin supplement for infants with cholestasis and other conditions associated with malabsorption of fat soluble vitamins.

**Dose & Administration**

20 to 80 mg/kg elemental calcium per day orally in divided doses scheduled around oral feedings.

**Calcium gluconate** 10% IV formulation (9.3 mg/mL elemental calcium): 2 to 8 mL/kg per day.

**Calcium carbonate** 250 mg/mL suspension (100 mg/mL elemental calcium): 0.2 to 0.8 mL/kg per day.

**Calcium glubionate** syrup (23 mg/mL elemental calcium): 1 to 3.5 mL/kg per day.

**Uses**

Treatment of non-acute hypocalcemia in babies able to tolerate oral medications.

**Monitoring**

Periodically measure serum calcium concentrations. Assess GI tolerance. Assess serum phosphorus and vitamin D levels when indicated.

**Adverse Effects/Precautions**

Oral calcium preparations are hypertonic, especially calcium glubionate syrup. Gastric irritation and diarrhea occur often. Use with caution in infants who are at risk for necrotizing enterocolitis.

**Pharmacology**

Absorption of calcium administered orally is approximately 50%. Absorption takes place throughout the small intestine, and is primarily regulated by 1,25-dihydroxy Vitamin D. Calcium carbonate significantly interferes with the absorption of levothyroxine. The osmolality of calcium glubionate syrup is 2500 mOsm/L, and of calcium gluconate is 700 mOsm/L.

**Special Considerations/Preparation**

Calcium carbonate (Roxane) is available as a 250 mg/mL suspension (equivalent to 100 mg/mL elemental calcium) in 5-mL unit dose cups. Calcium glubionate 6.5% syrup (Rugby/Watson) yields 23 mg/mL elemental calcium (1.16 mEq/mL) and is available in 473 mL bottles. Osmolality is 2500 mOsm/L.

**Selected References**

- ◆ Hsu SC, Levine MA: Perinatal calcium metabolism: physiology and pathophysiology. *Semin Neonat* 2004;9:23-36.
- ◆ Singh N, Weisler SL, Hershman JM: The acute effect of calcium carbonate on the intestinal absorption of levothyroxine. *Thyroid* 2001;11:967-71.
- ◆ Product information, Roxane, 1996.

Text updated 3/2008



**Dose & Administration**

**Symptomatic hypocalcemia - acute treatment:** 35 to 70 mg/kg per dose (0.35 to 0.7 mL/kg per dose, equivalent to 10 to 20 mg/kg elemental calcium).

Dilute in appropriate fluid, then infuse in IV over 10 to 30 minutes while monitoring for bradycardia. Stop infusion if heart rate is less than 100 beats per minute.

**Do not give intra-arterially.**

**Maintenance treatment:** 75 to 300 mg/kg per day (0.75 to 3 mL/kg per day, equivalent to 20 to 80 mg/kg elemental calcium). Administer by continuous IV infusion. Treat for 3 to 5 days, and follow serum concentrations periodically.

**Exchange transfusion:** 33 mg per 100 mL citrated blood exchanged (equals 0.33 mL per 100 mL blood exchanged). Infuse IV over 10 to 30 minutes.

**Uses**

Treatment and prevention of hypocalcemia, usually defined as a serum ionized calcium concentration less than approximately 4 mg/dL (or total serum calcium less than approximately 8 mg/dL).

**Monitoring**

If possible, measure ionized calcium directly. Avoid hypercalcemia during treatment. Correct hypomagnesemia if present. Observe IV infusion site closely for extravasation. Observe IV tubing for precipitates. Monitor continuously for bradycardia when giving bolus doses.

**Adverse Effects/Precautions**

Rapid administration is associated with bradycardia or cardiac standstill. Cutaneous necrosis or calcium deposition occurs with extravasation. Bolus infusions by UAC have been associated with intestinal bleeding and lower-extremity tissue necrosis.

**Pharmacology**

Calcium chloride may be more bioavailable than calcium gluconate, but it also is more likely to cause metabolic acidosis. Administration by continuous infusion is more efficacious than intermittent bolus dosing due to less renal calcium loss. Ionized calcium is the physiologically active fraction, accounting for approximately 50% of total blood calcium. The remainder is bound to albumin (40%) or complexed (10%) with citrate, phosphate, and bicarbonate. Early hypocalcemia is common in asphyxiated infants, premature infants, and infants of diabetic mothers. Significant decreases in ionized calcium may occur during acute alkalosis and following exchange transfusions with citrated blood. Clinical signs suggestive of hypocalcemia in neonates include muscle twitching, jitteriness, generalized seizures, and QTc above 0.4 second.

*continued...*

**Special Considerations/Preparation**

Calcium chloride 10% injection yields 27 mg/mL elemental calcium (1.36 mEq/mL). Osmolarity is 2040 mOsm/L. Injectable calcium salts should be stored at room temperature and are stable indefinitely.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Amikacin, amiodarone, chloramphenicol, dobutamine, dopamine, epinephrine, esmolol, hydrocortisone, isoproterenol, lidocaine, miconazole, milrinone, morphine, penicillin G, pentobarbital, phenobarbital, prostaglandin E<sub>1</sub>, and sodium nitroprusside.

**Incompatibility:** Amphotericin B, ceftriaxone, sodium bicarbonate, and phosphate and magnesium salts when mixed directly.

**Selected References**

- ◆ Zhou P, Markowitz M: Hypocalcemia in infants and children. *Pediatr Rev* 2009;30:190-2.
- ◆ Rigo J, DeCurtis M: Disorders of calcium, phosphorus, and magnesium metabolism. In: Martin RJ, Fanaroff AA, Walsh MC (eds): *Neonatal-Perinatal Medicine: Diseases of the Fetus and Newborn*, ed 8. St. Louis: Mosby, 2005, pp 1508-1514.
- ◆ Mimouni F, Tsang RC: Neonatal hypocalcemia: to treat or not to treat? (A review). *J Am Coll Nutr* 1994;13:408-15.
- ◆ Broner CW, Stidham GL, Westernkirchner DF, Watson DC: A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. *J Pediatr* 1990;117:986.
- ◆ Scott SM, Ladenson JH, Aguanza JJ, et al: Effect of calcium therapy in sick premature infants with early neonatal hypocalcemia. *J Pediatr* 1984;104:747.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 294.
- ◆ Product Information, Abbott, 2002

References updated 7/2010

Compatibilities updated 7/2009

**Dose & Administration**

**Symptomatic hypocalcemia - acute treatment:** 100 to 200 mg/kg per dose (1 to 2 mL/kg per dose, equivalent to 10 to 20 mg/kg elemental calcium).

Dilute in appropriate fluid, then infuse in IV over 10 to 30 minutes while monitoring for bradycardia. Stop infusion if heart rate is less than 100 beats per minute.

**Do not give intra-arterially.**

**Maintenance treatment:** 200 to 800 mg/kg per day (2 to 8 mL/kg per day, equivalent to 20 to 80 mg/kg elemental calcium).

Administer by continuous IV infusion. Treat for 3 to 5 days, and follow serum concentrations periodically.

**May also be given orally in the same dose.**

**Exchange transfusion:** 100 mg per 100 mL citrated blood exchanged (equals 1 mL per 100 mL blood exchanged). Infuse IV over 10 minutes.

**Uses**

Treatment and prevention of hypocalcemia, usually defined as a serum ionized calcium concentration less than approximately 4 mg/dL (or total serum calcium less than approximately 8 mg/dL). Treatment of asymptomatic infants is controversial.

**Monitoring**

If possible, measure ionized calcium directly. Avoid hypercalcemia during treatment. Correct hypomagnesemia if present. Observe IV infusion site closely for extravasation. Observe IV tubing for precipitates. Monitor continuously for bradycardia when giving bolus doses. Assess for GI intolerance when treating orally.

**Pharmacology**

Ionized calcium is the physiologically active fraction, accounting for approximately 50% of total blood calcium. The remainder is bound to albumin (40%) or complexed (10%) with citrate, phosphate, and bicarbonate. Early hypocalcemia is common in asphyxiated infants, premature infants, and infants of diabetic mothers. Significant decreases in ionized calcium may occur during acute alkalosis and following exchange transfusions with citrated blood. Clinical signs suggestive of hypocalcemia in neonates include muscle twitching, jitteriness, generalized seizures, and QT<sub>c</sub> above 0.4 second. Calcium chloride may be more bioavailable than calcium gluconate, but it also is more likely to cause metabolic acidosis. Administration by continuous infusion is more efficacious than intermittent bolus dosing due to less renal calcium loss.

*continued...*

**Special Considerations/Preparation**

Calcium gluconate 10% injection yields 9.3 mg/mL elemental calcium (0.46 mEq/mL). Osmolarity is 700 mOsm/L. Injectable calcium salts should be stored at room temperature and are stable indefinitely.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA solutions. Amikacin, aminophylline, amiodarone, ampicillin, aztreonam, caffeine citrate, cefazolin, cefepime, chloramphenicol, dobutamine, enalaprilat, epinephrine, famotidine, furosemide, heparin, hydrocortisone, lidocaine, linezolid, micafungin, midazolam, milrinone, netilmicin, nicardipine, penicillin G, phenobarbital, piperacillin-tazobactam, potassium chloride, propofol, remifentanyl, tobramycin, and vancomycin.

**Incompatibility:** Amphotericin B, ceftriaxone, fluconazole, indomethacin, meropenem, methylprednisolone, metoclopramide, and phosphate and magnesium salts when mixed directly.

**Selected References**

- ◆ Zhou P, Markowitz M: Hypocalcemia in infants and children. *Pediatr Rev* 2009;30:190-2.
- ◆ Jain A, Agarwal R, Sankar MJ, et al: Hypocalcemia in the newborn. *Indian J Pediatr* 2008;75:165-169.
- ◆ Rigo J, DeCurtis M: Disorders of calcium, phosphorus, and magnesium metabolism. In: Martin RJ, Fanaroff AA, Walsh MC (eds): *Neonatal-Perinatal Medicine: Diseases of the Fetus and Newborn*, ed 8. St. Louis: Mosby, 2005, pp 1508-1514.
- ◆ Porcelli PJ, Oh W: Effects of single dose calcium gluconate infusion in hypocalcemic preterm infants. *Am J Perinatol* 1995;12:18-21.
- ◆ Mimouni F, Tsang RC: Neonatal hypocalcemia: to treat or not to treat? (A review). *J Am Coll Nutr* 1994;13:408-15.
- ◆ Broner CW, Stidham GL, Westernkirchner DF, Watson DC: A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. *J Pediatr* 1990;117:986.
- ◆ Scott SM, Ladenson JH, Aguanza JJ, et al: Effect of calcium therapy in sick premature infants with early neonatal hypocalcemia. *J Pediatr* 1984;104:747.
- ◆ Tsang RC, Steichen JJ, Chang GM: Neonatal hypocalcemia: Mechanisms of occurrence and management. *Crit Care Med* 1977;5:56-61.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 294.
- ◆ Product Information, APP, 2002

References updated 7/2010

Compatibilities updated 7/2009

**Dose & Administration**

2 mg/kg per day of elemental iron for growing premature infants. (Maximum of 15 mg/day).

Begin therapy after 2 weeks of age.

Infants with birthweights less than 1000 grams may need 4 mg/kg per day.

6 mg/kg per day of elemental iron for patients receiving erythropoietin. Administer orally in 1 or 2 divided doses, preferably diluted in formula.

**Uses**

Iron supplementation for prevention and treatment of anemia.

**Monitoring**

Monitor hemoglobin and reticulocyte counts during therapy. Observe stools, check for constipation.

**Adverse Effects/Precautions**

In growing premature infants, iron supplementation should not be started until adequate vitamin E is supplied in the diet; otherwise, iron may increase hemolysis. Nausea, constipation, black stools, lethargy, hypotension, and erosion of gastric mucosa.

**Pharmacology**

Well absorbed from stomach.

**Special Considerations/Preparation**

**Drops:** Fer-In-Sol® drops now available as 15 mg elemental iron per 1 mL (0.2% alcohol) while other manufacturers FeSO<sub>4</sub> drops remain 15 mg elemental iron per 0.6 mL. **Confirm product concentration.**

**Elixir:** Contains 44 mg elemental iron per 5 mL (some with 5% alcohol).

**Selected References**

- ◆ Rao R, Georgieff M: Microminerals. In: Tsang R, Uauy R, Koletzko B, Zlotkin S. *Nutrition of the Preterm Infant. Scientific Basis and Practical Guidelines*. Cincinnati, Ohio: Digital Publishing Inc; 2005: pp 277-288.
- ◆ Rao R, Georgieff MK: Neonatal iron nutrition. *Semin Neonatol* 2001;6:425-35.
- ◆ Siimes MA, Järvenpää A-L: Prevention of anemia and iron deficiency in very low-birth-weight infants. *J Pediatr* 1982;101:277-280.
- ◆ Oski FA: Iron requirements of the premature infant, in Tsang R (ed): *Vitamin and Mineral Requirements in Preterm Infants*. New York: Marcel Dekker, 1985, p 18.
- ◆ Product Information, Mead Johnson, 2009

Special Considerations updated 1/2009

References updated 3/2007



**Dose & Administration**

**IV administration:** Infuvite® Pediatric is a sterile product consisting of two vials: a 4 mL vial labeled **Vial 1** and a 1 mL vial labeled **Vial 2**. The daily dose is a function of infant weight as indicated in the following table.

**Do not exceed this daily dose.**

**Infuvite Dosing**

	< 1 kg	≥ 1 kg and < 3 kg	≥ 3 kg
Vial 1	1.2 mL	2.6 mL	4 mL
Vial 2	0.3 mL	0.65 mL	1 mL

**Adverse Effects/Precautions**

**Warnings:** INFUVITE® Pediatric is administered in intravenous solutions, which may contain aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solution, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg per day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

**Pharmacology****INFUVITE® Pediatric**

Vial 1 (4 mL)	Amt*
Vitamin A** (as palmitate)	2300 IU (0.7 mg)
Vitamin D** (IU) (cholecalciferol)	400 IU (10 mcg)
Ascorbic Acid (vitamin C)	80 mg
Vitamin E** (dl-alpha tocopheryl acetate)	7 IU (7 mg)
Thiamine (as hydrochloride) B <sub>1</sub>	1.2 mg
Riboflavin (as phosphate) B <sub>2</sub>	1.4 mg
Niacinamide B <sub>3</sub>	17 mg
Pyridoxine hydrochloride B <sub>6</sub>	1 mg
d-Panthenol	5 mg
Vitamin K <sub>1</sub> **	0.2 mg
Vial 2 (1 mL)	
Biotin	20 mcg
Folic Acid	140 mcg
Vitamin B <sub>12</sub> (cyanocobalamin)	1 mcg

\* Amounts based upon guidelines published by the American Medical Association Department of Foods and Nutrition, JPEN 3(4);25862:1979.

**Vial 1 (4 mL) Inactive ingredients:** 50 mg polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for injection.

\*\* Polysorbate 80 is used to water solubilize the oil-soluble vitamins A, D, E, and K.

**Vial 2 (1 mL) Inactive ingredients:** 75 mg mannitol, citric acid and/or sodium citrate for pH adjustment and water for injection.

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**Special Considerations/Preparation**

After INFUVITE® *Pediatric* is diluted in an intravenous infusion, the resulting solution is ready for immediate use. Inspect visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Exposure to light should be minimized. Discard any unused portion. **Store between 2-8 °C (36-46 °F).**

**Incompatibility:** Direct addition to intravenous fat emulsions is not recommended.

**Selected References**

◆ Product Information, Baxter Clinitec 2001.

Compatibilities Updated 7/2009

Added 3/2002



**Dose & Administration**

0.4 to 1 mg/kg (400 to 1000 mcg/kg) per day IV continuous infusion in Dex/AA solutions containing at least 2% amino acids.

**Uses**

Iron supplementation in patients unable to tolerate oral iron, especially those also being treated with erythropoietin.

**Monitoring**

Periodic CBC and reticulocyte count. Observe Dex/AA solution for rust-colored precipitates.

**Adverse Effects/Precautions****Black Box Warning**

Anaphylactic-type reactions, including fatalities, have followed parenteral administration. Resuscitation equipment and trained personnel must be readily available during iron dextran administration.

No adverse effects have been observed in patients who have received low doses infused continuously. Large (50-mg) intramuscular doses administered to infants were associated with increased risk of infection. Retrospective reviews of adult patients who received larger doses injected over a few minutes report a 0.7% risk of immediate serious allergic reactions, and a 5% risk of delayed such as myalgia, arthralgia, phlebitis, and lymphadenopathy.

**Pharmacology**

Iron dextran for intravenous use is a complex of ferric hydroxide and low molecular mass dextran. The dextran serves as a protective lipophilic colloid. Radiolabeled iron dextran injected into adult subjects localized to the liver and spleen before being incorporated into RBC hemoglobin. Complete clearance occurred by 3 days. Approximately 40% of the labeled iron was bound to transferrin within 11 hours. The addition of iron dextran to Dex/AA solutions inhibits the spontaneous generation of peroxides.

**Special Considerations/Preparation**

Available as a 50 mg/mL concentration in 2-mL single-dose vials. Store at room temperature.

**Selected References**

- ◆ Mayhew SL, Quick MW: Compatibility of iron dextran with neonatal parenteral nutrition solutions. *Am J Health-Syst Pharm* 1997;54:570-1.
- ◆ Lavoie J-C, Chessex P: Bound iron admixture prevents the spontaneous generation of peroxides in total parenteral nutrition solutions. *J Pediatr Gastroenterol Nutr* 1997;25:307-11.
- ◆ Friel JK, Andrews WL, Hall MS, et al: Intravenous iron administration to very-low-birth-weight newborns receiving total and partial parenteral nutrition. *JPEN* 1995;19:114-18.
- ◆ Burns DL, Mascioli EA, Bistran BR: Parenteral iron dextran therapy: a review. *Nutrition* 1995;11:163-68.
- ◆ Kanakakorn K, Cavill I, Jacobs A: The metabolism of intravenously administered iron-dextran. *Br J Haematol* 1973;25:637-43.
- ◆ Product Information, Watson, 2009.

Adverse Effects/Precautions updated 12/2010

Special Considerations/Preparation updated 7/2009



**Dose & Administration****Resuscitation (Pulseless Torsades)**

25 to 50 mg/kg IV/intraosseous rapid infusion (over several minutes).

**Hypomagnesemia**

25 to 50 mg/kg IV infusion over 30 to 60 minutes; repeat dose as necessary. For hypomagnesemia/torsades with pulses, an infusion time of 10 to 20 minutes is recommended.

**Daily Maintenance Requirements (Parenteral Nutrition)**

0.25 to 0.5 mEq/kg/day IV.

**Administration**

Must be diluted prior to IV administration (10% to 20% solution (100 to 200 mg/mL)). Give by rapid infusion (over several minutes) for pulseless torsades, over 10 to 20 minutes for hypomagnesemia/torsades with pulses, and over 30 to 60 minutes for hypomagnesemia.

**Uses**

Treatment of torsades de pointes (polymorphic ventricular tachycardia associated with long QT interval). Treatment and prevention of hypomagnesemia. Treatment and prevention of magnesium deficiency in patients receiving total parenteral nutrition.

**Monitoring**

Monitor serum and urinary magnesium levels. Assess other electrolytes (calcium, potassium, phosphorus) and renal function periodically.

**Adverse Effects/Precautions**

**Contraindicated** in patients with heart block or myocardial damage. Hypotension and bradycardia may occur with rapid infusion. Calcium chloride should be available to reverse magnesium toxicity. Use with caution in patients with renal impairment since magnesium sulfate is eliminated renally. Respiratory depression may occur from high magnesium levels. Contains aluminum which may be toxic, especially in premature neonates and patients with renal impairment. Flushing, sweating, hypothermia, and stupor may occur.

**Pharmacology**

Magnesium is a cation of the intracellular fluid that is necessary for the activity of many enzyme systems and plays an important role in neurochemical transmission and muscular excitability. Approximately 99% of total body magnesium is in the intracellular compartment (bone, 85%; soft tissue and liver, 14%) and only 1% is present in the extracellular fluid. Because of this, serum concentrations do not adequately reflect total body magnesium stores. Most of the filtered magnesium (95%) is reabsorbed by the kidney. Magnesium deficiency leads to varied structural and functional abnormalities. Signs of hypomagnesemia include tetany, cardiac arrhythmia, decreased bone stability, apathy, and increased susceptibility to epileptic seizures. Magnesium deficiency is associated with hypocalcemia, hypokalemia, hypophosphatemia, decreased urinary magnesium and calcium levels, and decreased magnesium levels in cerebrospinal fluid, bone, muscle, and hematopoietic cells.

*continued...*

**Special Considerations/Preparation**

Supplied as 50% concentration in 2-, 10-, and 50-mL single dose vials containing 500 mg/mL of magnesium sulfate which provides 4.06 mEq each of magnesium and sulfate. Osmolarity is 4.06 mOsm/mL; pH range of 5.5 to 7.

**Solution Compatibility:** D<sub>5</sub>W, NS, LR, and Dex/AA solutions.

**Solution Incompatibility:** Fat emulsion.

**Terminal Injection Site Compatibility:** Acyclovir, amikacin, ampicillin, aztreonam, cefazolin, cefotaxime, cefoxitin, chloramphenicol, clindamycin, dobutamine, enalaprilat, erythromycin lactobionate, esmolol, famotidine, gentamicin, heparin sodium, hydrocortisone sodium succinate, insulin, linezolid, meropenem, metoclopramide, metronidazole, micafungin, milrinone, morphine, nafcillin, nicardipine, ondansetron, oxacillin, penicillin G potassium, piperacillin, piperacillin/tazobactam, potassium chloride, propofol, sodium nitroprusside, tobramycin, trimethoprim/sulfamethoxazole, and vancomycin.

**Incompatibility:** Amiodarone, amphotericin B, calcium chloride, cefepime, pantoprazole, and sodium bicarbonate.

**Selected References**

- ◆ American Academy of Pediatrics Committee on Nutrition. Parenteral Nutrition. In: Kleinman RE, ed. *Pediatric Nutrition Handbook* 2009, 6th ed.
- ◆ Assadi F: Hypomagnesemia. An evidence-based approach to clinical cases. *Iran J Kidney Dis* 2010;4:13-19.
- ◆ Chernow B, Smith J, Rainey TG, et al: Hypomagnesemia: Implications for the critical care specialist. *Crit Care Med* 1982;10:193-196.
- ◆ Hegenbarth MA, and the American Academy of Pediatrics Committee on Drugs: Preparing for pediatric emergencies: Drugs to consider. *Pediatrics* 2008;121:433-443.
- ◆ Hoshino K, Ogawa K, Hishitani T, et al: Optimal administration dosage of magnesium sulfate for Torsades de Pointes in children with long QT syndrome. *J Am Clin Nutr* 2004;2:497S-500S.
- ◆ Juan D: Clinical review: The clinical importance of hypomagnesemia. *Surgery* 1982;91:510-517.
- ◆ Kleinman ME, Chameides L, Schexnayder SM, et al: Part 14: Pediatric advanced life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122(suppl 3):S876-S908.
- ◆ Manrique AM, Arroyo M, Lin Y, et al: Magnesium supplementation during cardiopulmonary bypass to prevent junctional ectopic tachycardia after pediatric cardiac surgery: A randomized controlled study. *J Thorac Cardiovasc Surg* 2010;139:162-169.
- ◆ Mirtallo J, Canada T, Johnson D, et al: Safe practices for parenteral nutrition. *JPEN* 2004;28:S39-S70.
- ◆ Product Information: Magnesium sulfate injection, USP 50%, American Regent, 2009.
- ◆ Saleem AF, Haque A: On admission hypomagnesemia in critically ill children: Risk factors and outcome. *Indian J Pediatr* 2009;76:1227-1230.

Added 2/2011

**Dose & Administration**

**Initial oral replacement therapy:** 0.5 to 1 mEq/kg per day divided and administered with feedings (small, more frequent aliquots preferred). Adjust dosage based on monitoring of serum potassium concentrations.

$$1 \text{ g KCl} = 13.4 \text{ mEq K}^+$$

$$1 \text{ mEq K}^+ = 74.6 \text{ mg KCl}$$

**Acute treatment of symptomatic hypokalemia:** Begin with 0.5 to 1 mEq/kg IV over 1 hour, then reassess. **Maximum concentration:** 40 mEq/L for peripheral, 80 mEq/L for central venous infusions.

**Uses**

Treatment of hypokalemia.

**Monitoring**

**Continuous EKG monitoring is mandatory if administering by the IV route, especially for central infusions.** Observe IV site closely for signs of extravasation when using concentrated solutions. Monitor serum potassium concentration. Assess for GI intolerance.

**Adverse Effects/Precautions**

Rapid IV infusions, especially those through central lines, may cause arrhythmias including heart block and cardiac arrest. Peripheral IV administration of concentrated potassium solutions is associated with thrombophlebitis and pain at the injection site. GI irritation is common—most commonly diarrhea, vomiting, and bleeding—minimized by dividing oral doses and administering with feedings. Use with caution (if at all) in patients receiving potassium-sparing diuretics, e.g. spironolactone.

**Pharmacology**

Potassium is the major intracellular cation. Hypokalemia in critically ill neonates is usually the result of diuretic (furosemide, thiazides) therapy or diarrhea. Other causes include congenital adrenal hyperplasia and renal disorders. Alkalosis, as well as insulin infusions, will lower serum potassium concentrations by driving the ion intracellularly. Symptoms of hypokalemia include neuromuscular weakness and paralysis, ileus, urine retention, and EKG changes (ST segment depression, low-voltage T wave, and appearance of U wave). Hypokalemia increases digitalis toxicity. Oral potassium preparations are completely absorbed.

*continued...*

**Special Considerations/Preparation**

Potassium chloride for injection is supplied as 2-mEq/mL solution. **Always dilute before administration.** Hyperosmolar - 4355 mOsm/kg determined by freezing-point depression. pH ranges from 4 to 8 depending on buffering. Various oral solutions are available, with concentrations ranging from 10 to 40 mEq per 15 mL. Other oral forms available include powder packets, tablets, and sustained-release capsules.

**Solution Compatibility:** Most standard IV solutions.

**Terminal Injection Site Compatibility:** Most drugs.

**Incompatibility:** Amphotericin B, diazepam, and phenytoin.

**Selected References**

- ♦ Satlin LM, Schwartz GJ: Disorders of potassium metabolism, in Ichikawa I (ed): *Pediatric Textbook of Fluids and Electrolytes*. Baltimore: Williams & Wilkins, 1990, p 227.
- ♦ Morgan BC: Rapidly infused potassium chloride therapy in a child. *JAMA* 1981;245:2446.
- ♦ DeFronzo RA, Bia M: Intravenous potassium chloride therapy. *JAMA* 1981;245:2446.

Compatibilities updated 3/2007

Updated 3/1997

**Dose & Administration**

**Initial diagnostic dose:** 50 to 100 mg IV push, or IM.

**Maintenance dose:** 50 to 100 mg orally every 24 hours. High doses may be required during periods of intercurrent illness.

**Uses**

Diagnosis and treatment of pyridoxine-dependent seizures.

**Monitoring**

When possible, initial administration of pyridoxine should be accompanied by EEG monitoring.

**Adverse Effects/Precautions**

Risk of profound sedation. Ventilator support may be necessary.

**Pharmacology**

Pyridoxine-dependent seizures are a result of defective binding of pyridoxine in the formation of GABA (an inhibitory neurotransmitter). Administration of pharmacologic doses of pyridoxine will correct this GABA deficiency.

**Special Considerations/Preparation**

Injectable form available in concentration of 100 mg/mL (1 mL in 2-mL vial). May use injectable form orally; mix in simple syrup if desired.  
**Protect from light.**

**Solution Incompatibility:** Alkaline solutions. No data are currently available on Dex/AA.

**Incompatibility:** Iron salts and oxidizing agents. No data are currently available on heparin and potassium chloride.

**Selected References**

- ◆ Gospe SM: Current perspectives on pyridoxine-dependent seizures. *J Pediatr* 1998;132:919-923.
- ◆ Gordon N: Pyridoxine dependency: An update. *Dev Med Child Neurol* 1997;39:63.
- ◆ Mikati MA, Trevathan E, Krishnamoorthy KS, Lombroso CT: Pyridoxine-dependent epilepsy: Investigations and long-term followup. *Electroencephalogr Clin Neurophysiol* 1991;78:215.
- ◆ Kroll JS: Pyridoxine for neonatal seizures: An unexpected danger. *Dev Med Child Neurol* 1985;27:369.
- ◆ Bankier A, Turner M, Hopkins IJ: Pyridoxine-dependent seizures: A wider clinical spectrum. *Arch Dis Child* 1983;58:415.
- ◆ Product Information, Abraxis, 2006

Compatibilities updated 7/2009

**Dose & Administration**

1 dropperful (1 mL) every 24 hours, or as directed by physician.  
Percentages of the Reference Daily Intakes (%RDIs) listed in the table below are for infants.

**Vi-Sol® Products**

	Tri-Vi-Sol® Multivitamin Drops	Tri-Vi-Sol® Multivitamin with Iron Drops	Poly-Vi-Sol® Multivitamin Drops	Poly-Vi-Sol® Multivitamin with Iron Drops
	Amt (%RDI)	Amt (%RDI)	Amt (%RDI)	Amt (%RDI)
<b>Vitamins</b>				
A (IU)	1500 (100)	1500 (100)	1500 (100)	1500 (100)
D (IU)	400 (100)	400 (100)	400 (100)	400 (100)
C (mg)	35 (100)	35 (100)	35 (100)	35 (100)
E (IU)			5 (100)	5 (100)
Thiamine (B <sub>1</sub> ) (mg)			0.5 (100)	0.5 (100)
Riboflavin(B <sub>2</sub> ) (mg)			0.6 (100)	0.6 (100)
Niacin (mg)			8 (100)	8 (100)
B <sub>6</sub> (mg)			0.4 (100)	0.4 (100)
B <sub>12</sub> (mcg)			2 (100)	0*
<b>Minerals</b>				
Iron (mg)		10 (67)		10 (67)

\*Iron product contains no vitamin B12 due to instability with iron and vitamin C concentrations.



## (Retinyl Palmitate)

**Dose & Administration**

**Parenteral treatment of Vitamin A deficiency:** 5000 units IM 3 times weekly for 4 weeks.

Administer using 29-g needle and insulin syringe.

**DO NOT ADMINISTER IV.**

**Uses**

To reduce the risk of Chronic Lung Disease in high risk premature neonates with Vitamin A deficiency. In the NICHD-sponsored trial, 14 infants needed to be treated to prevent 1 case of Chronic Lung Disease.

**Monitoring**

Assess regularly for signs of toxicity: full fontanel, lethargy, irritability, hepatomegaly, edema, mucocutaneous lesions, and bony tenderness. Consider measuring plasma retinol concentrations if available, especially if patient is also receiving glucocorticoid therapy. Desired concentrations are approximately 30 to 60 mcg/dL. Concentrations less than 20 mcg/dL indicate deficiency, while those greater than 100 mcg/dL are potentially toxic.

**Adverse Effects/Precautions**

See monitoring section. Coincident treatment with glucocorticoids should be avoided, as it significantly raises plasma vitamin A concentrations.

**Pharmacology**

The pulmonary histopathologic changes of BPD and Vitamin A deficiency are remarkably similar. Vitamin A is the generic name for a group of fat soluble compounds which have the biological activity of the primary alcohol, retinol. Retinol metabolites exhibit potent and site-specific effects on gene expression and on lung growth and development. Retinol is supplied in the diet as retinyl esters.

**Special Considerations/Preparation**

Available as Aquasol A® Parenteral (water-miscible vitamin A palmitate) 50,000 units per mL, equivalent to 15 mg retinol per mL, in 2 mL vials.

**Protect from light.** Store refrigerated at 36 to 46 °F (2 to 8 °C). Do not freeze.

**Selected References**

- ◆ Tyson JE, Wright LL, Oh W, Kennedy K, et al: Vitamin A supplementation for extremely-low-birth-weight infants. *N Engl J Med* 1999;340:1962-68.
- ◆ Darlow BA, Graham PJ. Vitamin A supplementation for preventing morbidity and mortality in very low birthweight infants (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd.
- ◆ Shenai JP: Vitamin A supplementation in very low birthweight neonates: rationale and evidence. *Pediatrics* 1999;104:1369-74.
- ◆ Product information, Mayne, 2005

References updated 3/2003



**Dose & Administration**

**Supplementation:** 400 units per day orally.

**Treatment of vitamin D deficiency:** 1000 units per day orally.

**Uses**

Prevention and treatment of vitamin D deficiency. For breastfed infants, the AAP recommends that supplementation should begin within the first few days of life, regardless of whether the infant is exclusively breastfed or supplemented with infant formula. Exclusively formula-fed infants receiving at least 1000 mL/day of formula receive adequate amounts of vitamin D without supplementation. Recent data indicate that administration of high doses of vitamin D (4000 to 6400 units daily) to breastfeeding mothers is capable of raising 25(OH)-D levels in the infant to levels similar to those seen with infant supplementation without causing hypervitaminosis D in the mother.

**Monitoring**

Signs of vitamin D deficiency include symptomatic hypocalcemia (including seizures), growth failure, irritability, lethargy, and increased susceptibility for respiratory infections. A 25-hydroxyvitamin D (25(OH)-D) concentration of less than 50 nmol/L is thought to be indicative of vitamin D deficiency in infants.

**Adverse Effects/Precautions**

Signs of vitamin D toxicity include hypercalcemia, azotemia, vomiting, and nephrocalcinosis. A 25(OH)-D concentration greater than 250 nmol/L may be associated with a risk for vitamin D intoxication.

**Pharmacology**

The main source of vitamin D is vitamin D<sub>3</sub>, which is synthesized in the skin through exposure to ultraviolet B (UV-B) radiation. UV-B in the range of 290 to 315 nm initiates the synthesis of vitamin D<sub>3</sub> by converting 7-dehydrocholesterol into previtamin D<sub>3</sub>, which is further converted to vitamin D<sub>3</sub>. Vitamin D<sub>3</sub> binds to vitamin D-binding protein and is transported to the liver for 25-hydroxylation to 25(OH)-D (calcidiol). Calcidiol undergoes further hydroxylation in the kidney and other tissues to calcitriol (1,25-dihydroxyvitamin D) (1,25-OH<sub>2</sub>-D), the active form of vitamin D. Calcitriol stimulates the intestinal absorption of calcium and phosphorous, renal reabsorption of filtered calcium, and mobilization of calcium and phosphorous from bone. As a supplement, vitamin D<sub>3</sub> has been shown to be more effective in raising 25(OH)-D levels when compared with vitamin D<sub>2</sub>.

*continued...*

**Special Considerations/Preparation**

Vitamin D supplements are available as vitamin D<sub>2</sub> (ergocalciferol; plant derived) and vitamin D<sub>3</sub> (cholecalciferol; animal derived). Drisdol® (ergocalciferol oral solution) contains 200 units (5 mcg) vitamin D<sub>2</sub> per drop. The inactive ingredient is propylene glycol. Baby Ddrops™ (cholecalciferol liquid vitamin supplement) is supplied as 400 units vitamin D<sub>3</sub> per drop. The inactive ingredient is purified palm-kernel oil.

Bio-D-Mulsion™ (cholecalciferol; emulsified vitamin D<sub>3</sub>) is supplied as 400 units per drop. Inactive ingredients include water, sesame oil and acacia.

Just D (cholecalciferol) is supplied as 400 units vitamin D<sub>3</sub> per mL. The inactive ingredient is corn oil.

Enfamil® D-Vi-Sol™ (cholecalciferol) is supplied as 400 units vitamin D<sub>3</sub> per mL. Inactive ingredients include glycerin, water, polysorbate 80, citric acid, sodium citrate, sodium hydroxide, artificial flavor and artificial caramel color.

The vitamin D<sub>3</sub> content of Vi-Daylin® and Vi-Sol® products is 400 units per mL.

The vitamin D<sub>3</sub> content of AquADEKs™ drops is 400 units per mL.

**Selected References**

- ◆ American Academy of Pediatrics Committee on Nutrition: Vitamins. In: *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics 2009; pp 458, 464-466.
- ◆ Wagner CL, Greer FR and the Section on Breastfeeding and Committee on Nutrition: Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics* 2008;122:1142-1152.
- ◆ Misra M, Pacaud D, Petryk A et al: Vitamin D deficiency in children and its management: Review of current knowledge and recommendations. *Pediatrics* 2008;122:398-417.

Added 3/2009

**(dl-alpha-tocopherol acetate)****Dose & Administration**

5 to 25 units per day orally. Dilute with feedings. Do not administer simultaneously with iron—iron absorption is impaired.

**Uses**

Prevention of vitamin E deficiency. May be indicated in babies receiving erythropoietin and high iron dosages. Higher doses used to reduce oxidant-induced injury (ROP, BPD, IVH) remain controversial.

**Monitoring**

Assess feeding tolerance. Signs of vitamin E deficiency include hemolytic anemia and thrombocytosis. Physiologic serum vitamin E concentrations are between 0.8 and 3.5 mg/dL.

**Adverse Effects/Precautions**

Feeding intolerance may occur due to hyperosmolarity of preparation. Pharmacologic doses of alpha tocopherol have been associated with increased rates of sepsis (antioxidant effect of drug) and NEC (osmolarity of oral formulation).

**Pharmacology**

Alpha-tocopherol is the most active antioxidant of the group of tocopherols known as Vitamin E. The amount required by the body is primarily dependent upon the dietary intake of fat, especially polyunsaturated fatty acids (PUFA). Human milk and currently available infant formulas contain adequate Vitamin E and have appropriate E:PUFA ratios to prevent hemolytic anemia. Infants receiving supplemental iron amounts above 2 mg/kg/day may also require additional Vitamin E. Oral absorption of vitamin E is dependent upon hydrolysis that requires bile salts and pancreatic esterases. This can be quite variable in very immature infants and those with fat malabsorption. Free tocopherol is absorbed in the small intestine, taken via chylomicrons into the gastrointestinal lymphatics, then carried via low-density lipoproteins to be incorporated into cell membranes. Significant tissue accumulation may occur with pharmacologic doses.

**Special Considerations/Preparation**

Available as liquid drops: Aquavit E® (Cypress Pharmaceutical), 15 units (=15 mg) per 0.3 mL. Water solubilized with polysorbate 80. Also contains propylene glycol. Hyperosmolar (3620 mOsm/kg H<sub>2</sub>O). Store at controlled room temperature.

**Selected References**

- ◆ Gross SJ: Vitamin E. In Tsang RC, Lucas A, Uauy R, Zlotkin S (eds): *Nutritional Needs of the Preterm Infant: Scientific Basis and Practical Guidelines*. Pauling, New York: Caduceus Medical Publishers, 1993, pp 101-109.
- ◆ Roberts RJ, Knight ME: Pharmacology of vitamin E in the newborn. *Clin Perinatol* 1987;14:843-855.
- ◆ Raju TNK, Langenberg P, Bhutani V, Quinn GE: Vitamin E prophylaxis to reduce retinopathy of prematurity: A reappraisal of published trials. *J Pediatr* 1997;131:844-850.

Added 3/2001



**Dose & Administration**

**Recommended Prophylaxis:** 0.5 to 1 mg IM at birth.

**Preterm infants less than 32 weeks of gestation:**

**Birthweight greater than 1000 grams:** 0.5 mg IM.

**Birthweight less than 1000 grams:** 0.3 mg/kg IM.

**Alternate strategy for healthy, term, exclusively breast-fed infants:**

1 to 2 mg orally at birth, at 1 to 2 weeks of age, and at 4 weeks of age.

Oral prophylaxis is contraindicated in infants who are premature, ill, on antibiotics, have cholestasis, or have diarrhea. There has been an increased number of cases of hemorrhagic disease of the newborn in countries that have changed to oral prophylaxis, primarily in patients who received only a single oral dose.

Also: Maternal daily intake of 5 mg/day of phyloquinone significantly increases Vitamin K concentrations in breastmilk and infant plasma.

**Treatment of severe hemorrhagic disease:** 1 to 10 mg IV slow push.

(See Adverse Effects/Precautions for rate of administration.)

**Uses**

Prophylaxis and therapy of hemorrhagic disease of the newborn. Treatment of hypoprothrombinemia secondary to factors limiting absorption or synthesis of vitamin K<sub>1</sub>.

**Monitoring**

Check prothrombin time when treating clotting abnormalities. A minimum of 2 to 4 hours is needed for measurable improvement.

**Adverse Effects/Precautions**

Severe reactions, including death, have been reported with IV administration in adults. These reactions are extremely rare, and have resembled anaphylaxis and included shock and cardiac/respiratory arrest.

**With IV administration, give very slowly, not exceeding 1 mg per minute, with physician present.** Pain and swelling may occur at IM injection site. Efficacy of treatment with vitamin K<sub>1</sub> is decreased in patients with liver disease. The risk of childhood cancer is not increased by IM administration of vitamin K<sub>1</sub>.

**Note:** A box warning statement in the AquaMEPHYTON® product information states that intramuscular administration "should be restricted to those situations where the subcutaneous route is not feasible and the serious risk is considered justified". However, this does not apply to newborns, and the American Academy of Pediatrics recommends the single intramuscular dose at birth as above. The product information labeling reflects this recommended newborn dosing.

**Pharmacology**

Vitamin K<sub>1</sub> (phytonadione) promotes formation of the following clotting factors in the liver: active prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component (factor IX), and Stuart factor (factor X). Vitamin K<sub>1</sub> does **not** counteract the anticoagulant action of heparin.

*continued...*

**Special Considerations/Preparation**

Available as a 2 mg/mL aqueous dispersion in 0.5-mL ampules and 10 mg/mL aqueous dispersion in 1-mL ampules and 2.5- and 5-mL vials. Contains 0.9% (9 mg/mL) benzyl alcohol as a preservative.

\*\*\* Efficacy with giving this preparation orally is uncertain. \*\*\*

Protect from light.

An extemporaneous oral suspension can be made by triturating six 5-mg tablets in a mortar. While mixing, add 5 mL purified water, USP and 5 mL 1% methylcellulose. Transfer to a graduate and qs to 30 mL with 70% sorbitol solution. Final concentration is 1 mg/mL and suspension is stable for 3 days refrigerated. Shake well before using.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Amikacin, ampicillin, chloramphenicol, cimetidine, epinephrine, famotidine, heparin, hydrocortisone succinate, netilmicin, potassium chloride, ranitidine, and sodium bicarbonate.

**Incompatibility:** Dobutamine and phenytoin.

**Selected References**

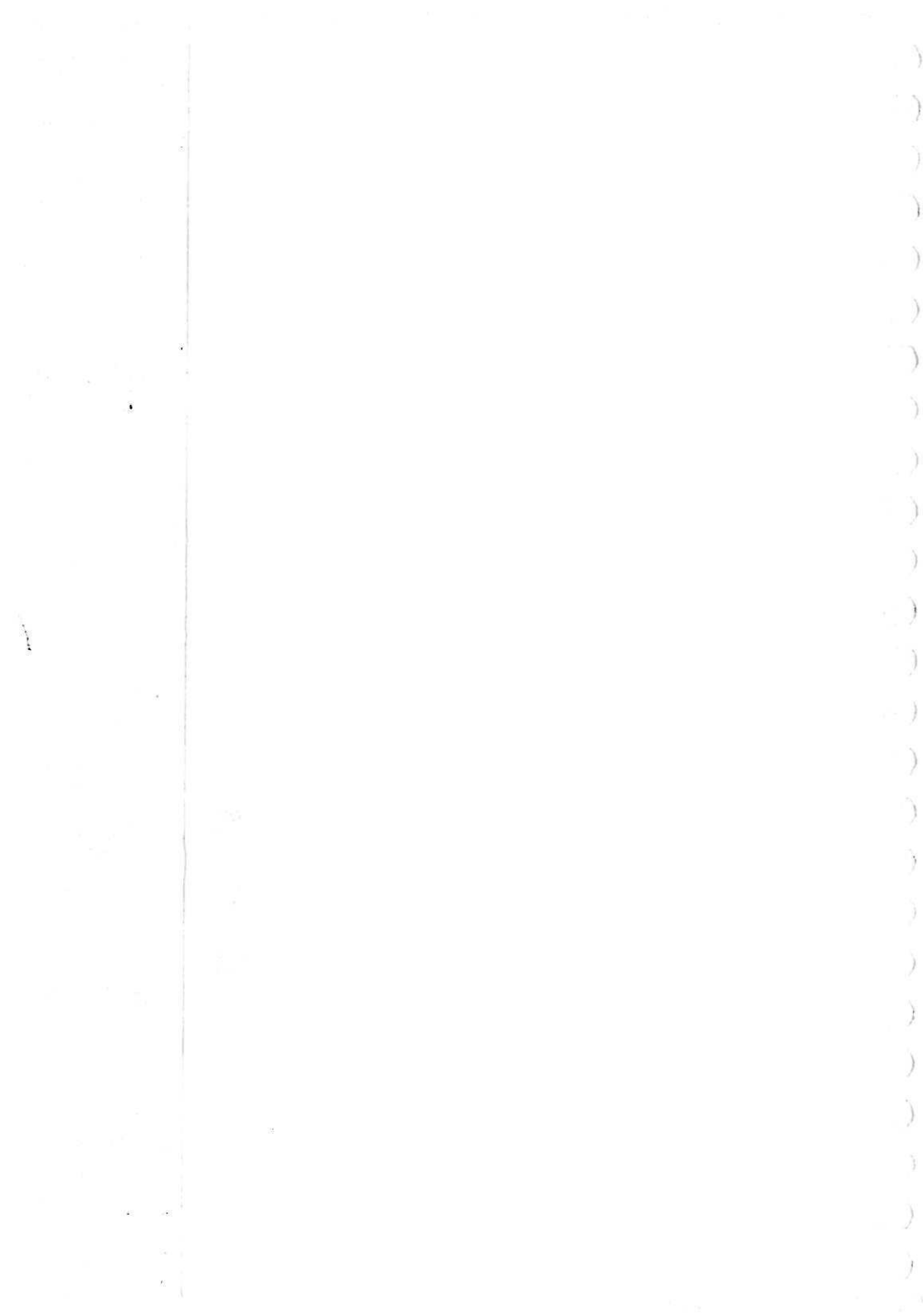
- ◆ American Academy of Pediatrics Committee on Nutrition: Vitamins. In: *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics 2009; pp 93, 468-471.
- ◆ Nahata MC, Pai VB, Hipple TF, eds. *Pediatric Drug Formulations*. 5th ed. Cincinnati, OH: Harvey Whitney Books Company; 2004:219.
- ◆ Costakos DT, Greer FR, Love LA, et al: Vitamin K prophylaxis for premature infants: 1 mg versus 0.5 mg. *Am J Perinatol* 2003;20:485-90.
- ◆ American Academy of Pediatrics, Committee on Fetus and Newborn: Controversies concerning vitamin K and the newborn. *Pediatrics* 2003;112:191-92.
- ◆ Kumar D, Greer FR, Super DM, et al: Vitamin K status of premature infants: implications for current recommendations. *Pediatrics* 2001;108:1117-1122.
- ◆ Fiore LD, Scola MA, Cantillon CE, Brophy MT: Anaphylactoid reactions to Vitamin K. *J Thromb Thrombolysis* 2001;11:175-188.
- ◆ Zipursky AL: Prevention of vitamin K deficiency bleeding in newborns. *Br J Haematol* 1999;104:430-437.
- ◆ Greer FR: Vitamin K deficiency and hemorrhage in infancy. *Clin Perinatol* 1995;22:759.
- ◆ Greer FR, Marshall SP, Foley AL, Suttie JW: Improving the vitamin K status of breastfeeding infants with maternal vitamin K supplements. *Pediatrics* 1997;99:88.
- ◆ Product Information, Hospira, 2004.
- ◆ Product Information, Aton Pharma, 2007.

Compatibilities updated 7/2009

Dosing and References updated 01/2009

Special Considerations updated 12/2008





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## NUTRITIONALS

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The following information, although accurate at the time of publication, is subject to change. The most current information may be obtained by referring to product packaging.

Potential renal solute load is estimated as follows:

$$[\text{Protein (g)} \times 5.714] + [\text{Na(mOsm)} + \text{K(mOsm)} + \text{Cl(mOsm)} + \text{P(mOsm)}]$$

Use the Powder-20 Dilution Table to reconstitute the following infant formulas from powder:

Enfamil® Gentlease®	Nutramigen® with Enflora™ LGG® **
Enfamil LIPIL®	Pregestimil® **
Enfamil® PREMIUM® Newborn	Similac® Advance®
Enfamil® PREMIUM® Infant	Similac Expert Care™ Alimentum®
Enfamil® Restfull™	Similac® Soy Isomil®
Enfamil A.R.®	Similac® Sensitive®
Enfamil® ProSobee®	Similac® Sensitive® for Spit-Up™
Good Start® Protect Plus®	Similac® PM 60/40
Nutramigen® **	Similac® Organic

**Dilution Table Powder-20**

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked (Scoopful)	Approximate Yield (fl oz)
20*	2	1	2
22	3.5	2	4
24	5	3	6
27	4.25	3	5

\* Standard mixture

\*\* Packed Level Scoopful

NOTE: Refer to 'Dilution Table Liquid-20' under 'Nutritionals' when mixing 40 Cal/fl oz concentrate.

Use the Powder-22 Dilution Table to reconstitute the following infant formulas from powder:

Enfamil® EnfaCare®	Similac® Expert Care™ NeoSure®
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**Dilution Table Powder-22**

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked (Scoopful)	Approximate Yield (fl oz)
20	4.5	2	5
22*	2	1	2
24	5.5	3	6
27	8	5	9

\* Standard mixture

Use the Liquid-20 Dilution Table to reconstitute the following infant formulas from (40 Cal/fl oz) liquid concentrate:

Enfamil LIPIL®	Nutramigen®
Enfamil® PREMIUM® Infant	Similac® Advance®
Enfamil® ProSobee®	Similac® Sensitive®
Good Start® Protect Plus®	Similac® Soy Isomil®

**Dilution Table Liquid-20**

Caloric Density (Cal/fl oz)	Water (fl oz)	Concentrated Liquid (fl oz)	Approximate Yield (fl oz)
20*	1	1	2
22	2.5	3	5.5
24	2	3	5
27	1	2	3

\* Standard mixture

Nutrient per Liter	Term*	Preterm
Energy, Cal	650-700	671
Volume, mL	1000	1000
Protein, g	9	14.09
% of total calories †	6	8
Fat, g	39.05	38.93
% of total calories ††	52	52
Linoleic acid, mg	3741	3691
Carbohydrate, g	79	66.4
% of total calories ‡	42	40
Water, g	898	879
<b>Minerals</b>		
Calcium, mg (mEq)	200-250 (13.9)	248 (12.4)
Phosphorus, mg (mEq)	120-140	128
Magnesium, mg	30-35	30.9
Iron, mg	0.3-0.9	1.21
Zinc, mg	1-3	3.42
Manganese, mcg	3	6
Copper, mcg	200-400	644
Molybdenum, mcg	—	—
Iodine, mcg	150	107
Selenium, mcg	7-33	14.8
Sodium, mg (mEq)	120-250 (10-12.5)	248 (10.8)
Potassium, mg (mEq)	400-550 (10-14)	570 (14.6)
Chloride, mg (mEq)	400-450 (10-13)	550 (15.5)
<b>Vitamins</b>		
Vitamin A, IU	2252	3899
Vitamin D, IU	20	20
Vitamin E, IU	4.1	10.7
Vitamin K, mcg	2-3	2
Thiamine (B <sub>1</sub> ), mcg	200	208
Riboflavin (B <sub>2</sub> ), mcg	400-600	483
Vitamin B <sub>6</sub> , mcg	90-310	148
Vitamin B <sub>12</sub> , mcg	0.5-1	0.47
Niacin, mcg	1800-6000	1503
Folic acid (Folacin), mcg	80-140	33
Pantothenic acid, mcg	2000-2500	1805
Biotin, mcg	5-9	4.0
Vitamin C (Ascorbic acid), mg	100	107
Choline, mg	95	94
Inositol, mg	149.7	147.7
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	97.6	125.6
Osmolality, mOsm/kg H <sub>2</sub> O	286	290
Osmolarity, mOsm/L	257	255

\* Composition of human milk varies with maternal diet, stage of lactation, within feedings, diurnally, and among mothers<sup>1,2</sup>. Values represent mature term milk (not colostrum or transitional milk). Total potentially available nucleotides = 72 mg/L<sup>3</sup>. The extent of bioavailability of all sources of nucleotides has not been determined.

<sup>1</sup> American Academy of Pediatrics Committee on Nutrition: Pediatric Nutrition Handbook, 6th ed. Elk Grove Village: American Academy of Pediatrics, 2009, 1201-1203.

<sup>2</sup> Lawrence RA: Breastfeeding: A Guide for the Medical Profession, 5th ed. St. Louis: Mosby Inc, 1999:136, 737.

<sup>3</sup> Leach JL, Baxter JH, Molitor BE, et al: Total potentially available nucleotides of human milk by stage of lactation. Am J Clin Nutr 1995;61:1224-1230.

† Protein Source: Mother's milk.

†† Fat Source: Mother's milk.

‡ Carbohydrate Source: Lactose, oligosaccharides.

## Preterm Human Milk + Similac® Human Milk Fortifier

1 pk/50 mL (adds an additional 2 Cal/fl oz)

1 pk/25 mL (adds an additional 4 Cal/fl oz)

Nutrient per Liter	1 pk/50 mL	1 pk/25 mL
Energy, Cal	731	790
Volume, mL	1000	1000
Protein, g	18.84	23.46
% of total calories †	10	12
Fat, g	40.18	41.41
% of total calories ††	49	47
Linoleic acid, mg	3642	3594
Carbohydrate, g	74.4	82.2
% of total calories ‡	41	42
Water, g	867	856
<b>Minerals</b>		
Calcium, mg (mEq)	822 (41)	1381 (68.9)
Phosphorus, mg (mEq)	456 (14.6)	777 (24.9)
Magnesium, mg	65	98.2
Iron, mg	2.92*	4.58*
Zinc, mg	8.31	13.07
Manganese, mcg	41	76
Copper, mcg	1474	2283
Molybdenum, mcg	—	—
Iodine, mcg	106	105
Selenium, mcg	17	19.2
Sodium, mg (mEq)	319 (13.9)	388 (16.9)
Potassium, mg (mEq)	874 (22.3)	1169 (29.9)
Chloride, mg (mEq)	730 (20.6)	906 (25.5)
<b>Vitamins</b>		
Vitamin A, IU	6906	9834
Vitamin D, IU	612	1188
Vitamin E, IU	26.4	41.6
Vitamin K, mcg	42.9	82.8
Thiamine (B <sub>1</sub> ), mcg	1355	2471
Riboflavin (B <sub>2</sub> ), mcg	2534	4531
Vitamin B <sub>6</sub> , mcg	1187	2198
Vitamin B <sub>12</sub> , mcg	3.62	6.69
Niacin, mcg	19096	36225
Folic acid (Folacin), mcg	146	256
Pantothenic acid, mcg	9181	16364
Biotin, mcg	132.2	257.1
Vitamin C (Ascorbic acid), mg	229	348
Choline, mg	102	109
Inositol, mg	164.7	181.3
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	179.2	231.5
Osmolality, mOsm/kg H <sub>2</sub> O	343 (est.)	385 (est.)
Osmolarity, mOsm/L	297	329

\* Additional iron may be supplied from other sources as necessary.

† Protein Source: Preterm human milk, nonfat milk, and whey protein concentrate.

†† Fat Source: Preterm human milk and MCT oil.

‡ Carbohydrate Source: Lactose and corn syrup solids.

**Precaution:** Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Similac® Human Milk Fortifier can be added to human milk.

# Preterm Human Milk + Enfamil® Human Milk Fortifier

375

1 pk/50 mL (22 Cal/fl oz)

1 pk/25 mL (24 Cal/fl oz)

Nutrient per Liter	1 pk/50 mL	1 pk/25 mL
Energy, Cal	739	803
Volume, mL	1000	1000
Protein, g	19.6	25
% of total calories †	11	12
Fat, g	43.9	48.7
% of total calories ††	54	55
Linoleic acid, mg	4391	5070
Carbohydrate, g	68.4	70
% of total calories ‡	37	35
Water, g	879	874
<b>Minerals</b>		
Calcium, mg (mEq)	698 (34.8)	1147 (57.2)
Phosphorus, mg (mEq)	378	627
Magnesium, mg	36	41
Iron, mg	8.41*	15.6*
Zinc, mg	7.02	10.6
Manganese, mcg	56	106
Copper, mcg	864	1080
Molybdenum, mcg	—	—
Iodine, mcg	—	—
Selenium, mcg	—	—
Sodium, mg (mEq)	328 (14.3)	407 (17.7)
Potassium, mg (mEq)	715 (18.3)	857 (21.9)
Chloride, mg (mEq)	615 (17.3)	677 (19.1)
<b>Vitamins</b>		
Vitamin A, IU	8649	13377
Vitamin D, IU	770	1520
Vitamin E, IU	33.7	56.6
Vitamin K, mcg	24	46
Thiamine (B <sub>1</sub> ), mcg	958	1707
Riboflavin (B <sub>2</sub> ), mcg	1583	2680
Vitamin B <sub>6</sub> , mcg	723	1297
Vitamin B <sub>12</sub> , mcg	1.37	2.27
Niacin, mcg	16503	31494
Folic acid (Folacin), mcg	158	283
Pantothenic acid, mcg	5455	9095
Biotin, mcg	19.5	33
Vitamin C (Ascorbic acid), mg	170	229
Choline, mg	—	—
Inositol, mg	—	—
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	174	221.8
Osmolality, mOsm/kg H <sub>2</sub> O	308	325
Osmolarity, mOsm/L	270	284

\* Additional iron may be supplied from other sources as necessary.

† Protein Source: Mature preterm human milk, whey protein concentrate, and sodium caseinate.

†† Fat Source: Preterm human milk and corn syrup solids.

‡ Carbohydrate Source: Lactose.

**Precautions:** Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Enfamil® Human Milk Fortifier can be added to human milk.

## Preparation:

24 Cal/fl oz = 2 pks + 48 mL Mature Preterm Human Milk (yield 1.6 fl oz)

24 Cal/fl oz = 2 pks + 60 mL Term Human Milk (yield 2 fl oz)

## Preterm Human Milk + Prolact+ H<sup>2</sup>MF™ Human Milk Fortifier

**Prolact+ 4 H<sup>2</sup>MF™** formulated to meet target of 4 Cal/fl oz. Fortifies breast milk up to 2.3 g of protein in 100 mL of nutrition.

**Prolact+ 6 H<sup>2</sup>MF™** formulated to meet target of 6 Cal/fl oz. Fortifies breast milk up to 2.8 g of protein in 100 mL of nutrition.

**Prolact+ 8 H<sup>2</sup>MF™** formulated to meet target of 8 Cal/fl oz. Fortifies breast milk up to 3.2 g of protein in 100 mL of nutrition.

**Prolact+ 10 H<sup>2</sup>MF™** formulated to meet target of 10 Cal/fl oz. Fortifies breast milk up to 3.7 g of protein in 100 mL of nutrition.

Nutrient per 100 mL	Preterm Milk	Prolact+4	Prolact+6	Prolact+8	Prolact+10
Mixing ratios	n/a	4:1	7:3	3:2	1:1
BM:H <sup>2</sup> MF					
Energy, cal	67	83	91	98	104
Protein (human), g	1.4	2.3	2.8	3.2	3.7
Carbohydrate, g	6.6	7.3	7.6	8	7.8
Fat (human), g	3.9	4.9	5.4	5.9	6.5
<b>Minerals</b>					
Sodium, mg	25	54	54	54	61
Potassium, mg	57	71	71	71	75
Calcium, mg	25	128	128	128	154
Phosphorus, mg	12.8	70	70	70	86
Magnesium, mg	3.1	8	8	8	9
Chloride, mg	55	83	83	83	91
Manganese, mcg	0.7	2.4	2.4	2.4	2.8
Copper, mcg	64	67	67	67	68
Zinc, mg	0.34	0.74	0.74	0.74	0.84
Iron, mg	0.12	0.2	0.2	0.2	0.2
<b>Osmolality,</b>					
mOsm/kg H <sub>2</sub> O	~290	<335	<360	<325	<350
<b>Fatty Acids*</b>					
Linoleic acid, mg		250	375	500	625
Linolenic acid, mg		2	3	4	5
Arachadonic acid, mg		6.6	9.8	13.1	16.5
Docosahexaenoic acid, mg		2	3	4	5

\* Fatty acid data for preterm human milk is not available. Values shown represent levels of nutrients found in Prolact+ fortifiers.

Enfamil® Human Milk Fortifier

Nutrient	per 1 pk	per 4 pks
Energy, Cal	3.38	13.53
Protein, g	0.28	1.1
Fat, g	0.25	1
Linoleic acid, mg	35	140
Carbohydrate, g	<0.1	<0.4
<b>Minerals</b>		
Calcium, mg (mEq)	23 (1.12)	90 (4.49)
Phosphorus, mg (mEq)	12.5 (0.4)	50 (1.61)
Magnesium, mg	0.25	1
Iron, mg	0.36*	1.44*
Zinc, mg	0.18	0.72
Manganese, mcg	2.5	10
Copper, mcg	11	44
Iodine, mcg	-	-
Selenium, mcg	-	-
Sodium, mg (mEq)	4 (0.17)	16 (0.7)
Potassium, mg (mEq)	7.3 (0.19)	29 (0.74)
Chloride, mg (mEq)	3.3 (0.09)	13 (0.37)
<b>Vitamins</b>		
Vitamin A, IU	238	950
Vitamin D, IU	38	150
Vitamin E, IU	1.15	4.6
Vitamin K, mcg	1.1	4.4
Thiamine (B <sub>1</sub> ), mcg	38	150
Riboflavin (B <sub>2</sub> ), mcg	55	220
Vitamin B <sub>6</sub> , mcg	29	115
Vitamin B <sub>12</sub> , mcg	0.05	0.18
Niacin, mcg	750	3000
Folic acid (Folacin), mcg	6.3	25
Pantothenic acid, mcg	183	730
Biotin, mcg	0.68	2.7
Vitamin C (Ascorbic acid), mg	3	12
<b>Renal Solute Load, mOsm</b>	2.4	9.7

\* Additional iron should be supplied from other sources.

**Precautions:** Nutritionally incomplete. Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Enfamil Human Milk Fortifier can be added.



## Similac® Human Milk Fortifier

Nutrient	per 1 pk	per 4 pks
Energy, Cal	3.5	14
Protein, g	0.25	1
Fat, g	0.09	0.36
Linoleic acid, mg	-	-
Carbohydrate, g	0.45	1.8
<b>Minerals</b>		
Calcium, mg (mEq)	29.25 (1.46)	117 (5.84)
Phosphorus, mg (mEq)	16.8 (0.54)	67 (2.16)
Magnesium, mg	1.75	7
Iron, mg	0.08*	0.35*
Zinc, mg	0.25	1
Manganese, mcg	1.8	7.2
Copper, mcg	42.5	170
Iodine, mcg	-	-
Selenium, mcg	-	-
Sodium, mg (mEq)	3.75 (0.16)	15 (0.65)
Potassium, mg (mEq)	15.75 (0.4)	63 (1.61)
Chloride, mg (mEq)	9.5 (0.27)	38 (1.07)
<b>Vitamins</b>		
Vitamin A, IU	155	620
Vitamin D, IU	30	120
Vitamin E, IU	0.8	3.2
Vitamin K, mcg	2.1	8.3
Thiamine (B <sub>1</sub> ), mcg	58.3	233
Riboflavin (B <sub>2</sub> ), mcg	104	417
Vitamin B <sub>6</sub> , mcg	53	211
Vitamin B <sub>12</sub> , mcg	0.16	0.64
Niacin, mcg	893	3570
Folic acid (Folacin), mcg	5.75	23
Pantothenic acid, mcg	375	1500
Biotin, mcg	6.5	26
Vitamin C (Ascorbic acid), mg	6.3	25
Choline, mg	0.5	2
Inositol, mg	1	4
<b>Renal Solute Load, mOsm</b>	<b>2.8</b>	<b>11.2</b>

\* Additional iron should be supplied from other sources.

**Precautions:** Nutritionally incomplete. Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Similac Human Milk Fortifier can be added.

## **Prolact+ H<sup>2</sup>MF™ Human Milk Fortifier (Human, Pasteurized)**

**Prolact+ 4 H<sup>2</sup>MF™** formulated to meet target of 4 Cal/fl oz. Fortifies breast milk up to 2.3 g of protein in 100 mL of nutrition.

**Prolact+ 6 H<sup>2</sup>MF™** formulated to meet target of 6 Cal/fl oz. Fortifies breast milk up to 2.8 g of protein in 100 mL of nutrition.

**Prolact+ 8 H<sup>2</sup>MF™** formulated to meet target of 8 Cal/fl oz. Fortifies breast milk up to 3.2 g of protein in 100 mL of nutrition.

**Prolact+ 10 H<sup>2</sup>MF™** formulated to meet target of 10 Cal/fl oz. Fortifies breast milk up to 3.7 g of protein in 100 mL of nutrition.

Nutrient	Prolact+4	Prolact+6	Prolact+8	Prolact+10
Energy, kcal <sup>1</sup>	141	141	141	141
Volume, mL	100	100	100	100
Protein, g <sup>2</sup>	6	6	6	6
% of total kcal <sup>3</sup>	17%	17%	17%	17%
Fat, g <sup>2</sup>	9	9	9	9
% of total calories <sup>3</sup>	57%	57%	57%	57%
Carbohydrate, g <sup>4</sup>	9.1	9.1	9.1	9.1
% of total calories <sup>3</sup>	26%	26%	26%	26%
<b>Minerals</b>				
Calcium, mg <sup>2</sup>	588	400	306	250
Phosphorus, mg <sup>2</sup>	348	236	181	147
Magnesium, mg <sup>2</sup>	25.6	18.1	14.4	12.1
Iron, mg <sup>4</sup>	0.5	0.5	0.5	0.5
Zinc, mg <sup>2</sup>	2.7	1.9	1.5	1.3
Manganese, mcg <sup>4</sup>	<60	<60	<60	<60
Copper, mcg <sup>2</sup>	304	224	184	160
Sodium, mg <sup>2</sup>	185	132	105	89
Potassium, mg <sup>2</sup>	172	134	115	103
Chloride, mg <sup>2</sup>	193	147	124	110
<b>Vitamins</b>				
Vitamin A, IU <sup>4</sup>	298	298	298	298
Vitamin D, IU <sup>5</sup>	130	130	130	130
Vitamin E, IU <sup>5</sup>	2	2	2	2
Vitamin K, mcg <sup>5</sup>	<1	<1	<1	<1
Thiamine B <sub>1</sub> , mcg <sup>5</sup>	20	20	20	20
Riboflavin B <sub>2</sub> , mcg <sup>5</sup>	75	75	75	75
Niacin, mcg <sup>5</sup>	262	262	262	262
Folic acid, mcg <sup>5</sup>	27	27	27	27
Pantothenic Acid, mcg <sup>5</sup>	374	374	374	374
Biotin, mcg <sup>5</sup>	0.9	0.9	0.9	0.9
Vitamin C, mg <sup>4</sup>	<1	<1	<1	<1

<sup>1</sup> Derived from protein, carbohydrate, and fat [Atwater factors].

<sup>2</sup> Manufacturing target for Prolact+ fortifiers.

<sup>3</sup> Calories from component divided by total energy.

<sup>4</sup> Based on historical data of Prolact+ fortifier lots.

<sup>5</sup> Naturally occurring in milk after pasteurization. Based on specific testing from three lots.

# Preterm Human Milk + Similac® Special Care® 30 (1:1 ratio)

25 Cal/fl oz (approximate)

Based on mean nutrient concentrations in human milk.

Nutrient	per 100 Cal	per 100 mL
Energy, Cal	100	84.3
Volume, mL	119	100
Protein, g	2.64	2.23
% of total calories †	—	—
Fat, g	6.29	5.3
% of total calories ††	—	—
Linoleic acid, mg	640	540
Carbohydrate, g	8.6	7.24
% of total calories ‡	—	—
Water, g	—	—
<b>Minerals</b>		
Calcium, mg (mEq)	123	103.7
Phosphorus, mg (mEq)	68	57.1
Magnesium, mg	9.1	7.6
Iron, mg	1.15	0.97
Zinc, mg	1.11	0.93
Manganese, mcg	8	6.4
Copper, mcg	189	159
Molybdenum, mcg	—	—
Iodine, mcg	10	8
Selenium, mcg	—	—
Sodium, mg (mEq)	41	34
Potassium, mg (mEq)	111	94
Chloride, mg (mEq)	81	69
<b>Vitamins</b>		
Vitamin A, IU	984	829
Vitamin D, IU	91	77
Vitamin E, IU	3	2.6
Vitamin K, mcg	7.3	6.2
Thiamine (B <sub>1</sub> ), mcg	163	137
Riboflavin (B <sub>2</sub> ), mcg	402	339
Vitamin B <sub>6</sub> , mcg	159	134
Vitamin B <sub>12</sub> , mcg	0.36	0.3
Niacin, mcg	3098	2611
Folic acid (Folacin), mcg	24	20.4
Pantothenic acid, mcg	1251	1054
Biotin, mcg	22.5	19
Vitamin C (Ascorbic acid), mg	29	24.1
Choline, mg	12	9.8
Inositol, mg	33	27.7
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	24.2	20.4
Osmolality, mOsm/kg H <sub>2</sub> O	—	310
Osmolarity, mOsm/L	310 (est.)	—

† Protein Source: Preterm human milk, nonfat milk and whey protein concentrate.

†† Fat Source: Preterm human milk, medium chain triglycerides, soy and coconut oils.

‡ Carbohydrate Source: Preterm human milk, corn syrup solids, lactose.

When combined with human milk, does not increase concentrations of nutrients to levels achieved with Similac® Human Milk Fortifier.

# Term Human Milk + Similac® NeoSure® Powder

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Term Human Milk + Similac® NeoSure® Powder \*

Nutrient per 100 mL	22 Cal/fl oz	24 Cal/fl oz	27 Cal/fl oz
Energy, Cal	76	83	93
Protein, g	1.27	1.45	1.73
% of total calories †	6.7	7	7.4
Fat, g	4.33	4.7	5.27
% of total calories ††	51.4	51.2	51
Linoleic acid, mg	435	486	567
Carbohydrate, g	8.01	8.69	9.77
% of total calories ‡	42.2	42.1	42
Water, g	87	86	87
<b>Minerals</b>			
Calcium, mg	37	44	56
Phosphorus, mg (mEq)	19	24	31
Magnesium, mg (mEq)	4.2	4.9	5.9
Iron, mg	0.19	0.32	0.53
Zinc, mg	0.22	0.31	0.45
Manganese, mcg	1	2	3
Copper, mcg	35	44	57
Molybdenum, mcg	-	-	-
Iodine, mcg	12	13	15
Selenium, mcg	1.7	1.8	2.1
Sodium, mg (mEq)	21	23	26
Potassium, mg (mEq)	65	74	90
Chloride, mg (mEq)	48	53	61
<b>Vitamins</b>			
Vitamin A, IU	263	294	344
Vitamin D, IU	8	13	21
Vitamin E, IU	0.7	1	1.4
Vitamin K, mcg	1.2	2	3.3
Thiamine (B <sub>1</sub> ), mcg	40	56	81
Riboflavin (B <sub>2</sub> ), mcg	48	58	75
Vitamin B <sub>6</sub> , mcg	29	36	47
Vitamin B <sub>12</sub> , mcg	0.08	0.11	0.16
Niacin, mcg	320	461	685
Folic acid, mcg	7.1	8.9	11.7
Pantothenic acid, mcg	248	305	395
Biotin, mcg	1.2	1.8	2.9
Vitamin C, mg	5	6	8
Choline, mg	10	12	13
Inositol, mg	18	20	24
L-Carnitine, mg	-	-	-
Taurine, mg	-	-	-
Nucleotide fortification, mg	-	-	-
Renal Solute Load, mOsm	11.9	13.6	16.3
Osmolality, mOsm/kg H <sub>2</sub> O	-	-	-
Osmolarity, mOsm/L	-	-	-

\* Nutrient needs of small premature infants may not be met by this fortification strategy. Compare nutrient profile to fortification with Similac Human Milk Fortifier.

† Protein Source: Term human milk, nonfat milk and whey protein concentrate.

†† Fat Source: High-oleic safflower, soy, MCT, coconut, Term human milk, and C.cohnii<sup>1</sup> and M. alpina<sup>2</sup> oils.

<sup>1</sup> A source of docosahexaenoic acid (DHA).

<sup>2</sup> A source of arachidonic acid (ARA).

‡ Carbohydrate Source: Lactose, maltodextrin.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Preparation:

22 Calorie = 1 tsp level powder + 130 mL Term Human Milk

24 Calorie = 1 tsp level powder + 70 mL Term Human Milk

27 Calorie = 1 tsp level powder + 40 mL Term Human Milk

NEOFAX® 2011

# Term Human Milk + EnfaCare® LIPIL® Powder

Term Human Milk + EnfaCare® LIPIL® Powder \*

Nutrient per 100 mL	22 Cal/fl oz	24 Cal/fl oz	27 Cal/fl oz
Energy, Cal	74	81	91
Protein, g	1.34	1.54	1.85
% of total calories †	6.6	7.1	7.6
Fat, g	4.24	4.6	5.13
% of total calories ††	51.3	51	50.6
Linoleic acid, mg	438	505	606
Carbohydrate, g	8.3	9	10.1
% of total calories ‡	42.3	42.2	42.1
Water, g	89	88	86
<b>Minerals</b>			
Calcium, mg (mEq)	35 (1.8)	43 (2.2)	57 (2.9)
Phosphorus, mg (mEq)	17.1 (0.5)	22 (0.7)	29 (0.9)
Magnesium, mg	4	4.6	5.4
Iron, mg	0.15	0.29	0.49
Zinc, mg	0.21	0.3	0.44
Manganese, mcg	1.8	2.9	4.5
Copper, mcg	33	42	55
Molybdenum, mcg	-	-	-
Iodine, mcg	12	14	16
Selenium, mcg	1.7	1.9	2.2
Sodium, mg (mEq)	17.5 (0.8)	20 (0.9)	24 (1.1)
Potassium, mg (mEq)	58 (1.5)	65 (1.6)	76 (1.9)
Chloride, mg (mEq)	47 (1.3)	53 (1.5)	61 (1.7)
<b>Vitamins</b>			
Vitamin A, IU	255	286	333
Vitamin D, IU	7.6	13.6	22.6
Vitamin E, IU	0.69	0.98	1.43
Vitamin K, mcg	0.76	1.36	2.26
Thiamine (B <sub>1</sub> ), mcg	35	50	72
Riboflavin (B <sub>2</sub> ), mcg	49	63	85
Vitamin B <sub>6</sub> , mcg	27	35	45
Vitamin B <sub>12</sub> , mcg	0.07	0.09	0.12
Niacin, mcg	290	439	661
Folic acid (Folacin), mcg	6.6	8.5	11.3
Pantothenic acid, mcg	239	300	393
Biotin, mcg	0.83	1.28	1.94
Vitamin C (Ascorbic acid), mg	5.2	6.3	8.1
Choline, mg	11	13	15
Inositol, mg	17	19	22
L-Carnitine, mg	-	-	-
Taurine, mg	-	-	-
Nucleotide fortification, mg	0.3	0.61	1.08
Renal Solute Load, mOsm	11.4	13.1	15.7
Osmolality, mOsm/kg H <sub>2</sub> O	308	332	368
Osmolarity, mOsm/L	274	292	319

\* Nutrient needs of small premature infants may not be met by this fortification strategy. Compare nutrient profile to fortification with Enfamil Human Milk Fortifier.

† Protein Source: Term human milk, nonfat milk and whey protein concentrate.

†† Fat Source: High-oleic vegetable, soy, MCT, coconut, and C. cohnii<sup>1</sup> and M. alpina<sup>2</sup> oils.

<sup>1</sup> A source of docosahexaenoic acid (DHA).

<sup>2</sup> A source of arachidonic acid (ARA).

‡ Carbohydrate Source: Lactose, maltodextrin.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Preparation:

22 Calorie = 1/4 tsp packed powder + 45 mL Human Milk

24 Calorie = 1/2 tsp packed powder + 45 mL Human Milk

27 Calorie = 1 tsp packed powder + 45 mL Human Milk

Similac® Special Care® 20 with Iron Premature Infant Formula \*  
 Similac® Special Care® 20 Low Iron Premature Infant Formula \*\*  
 20 Cal/fl oz  
 Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3	20.29
% of total calories †	12	12
Fat, g	5.43	36.72
% of total calories ††	47	47
Linoleic acid, mg	700	4734
Carbohydrate, g	10.3	69.7
% of total calories ‡	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	180 (9)	1217 (60.7)
Phosphorus, mg (mEq)	100 (3.2)	676 (21.8)
Magnesium, mg	12	81.2
Iron, mg	1.8* (0.37)**	12.2* (2.5)**
Zinc, mg	1.5	10.14
Manganese, mcg	12	81
Copper, mcg	250	1691
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	43 (1.9)	291 (12.6)
Potassium, mg (mEq)	129 (3.3)	872 (22.3)
Chloride, mg (mEq)	81 (2.3)	548 (15.5)
<b>Vitamins</b>		
Vitamin A, IU	1250	8454
Vitamin D, IU	150	1014
Vitamin E, IU	4	27.1
Vitamin K, mcg	12	81.2
Thiamine (B <sub>1</sub> ), mcg	250	1691
Riboflavin (B <sub>2</sub> ), mcg	620	4193
Vitamin B <sub>6</sub> , mcg	250	1691
Vitamin B <sub>12</sub> , mcg	0.55	3.72
Niacin, mcg	5000	33815
Folic acid (Folacin), mcg	37	250
Pantothenic acid, mcg	1900	12850
Biotin, mcg	37	250
Vitamin C (Ascorbic acid), mg	37	250
Choline, mg	10	68
Inositol, mg	40	271
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	10.7	72.4
Renal Solute Load, mOsm	27.8	188.2
Osmolality, mOsm/kg H <sub>2</sub> O	235	235
Osmolarity, mOsm/L	211	211

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

\*\* Low-iron: Additional iron should be supplied from other sources.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: Medium chain triglyceride, soy, and coconut oils (0.25% DHA; 0.4% ARA).

‡ Carbohydrate Source: Corn syrup solids and lactose.

**Precautions:** Tolerance to enteral feedings should be confirmed by initially offering small volumes of hypocaloric formula followed by cautious progression to higher caloric feedings. Spitting up, excessive gastric residuals, abdominal distention, abnormal stools or stool patterns, or other signs of intestinal dysfunction have been associated with enteral feeding before the intestinal tract is ready to accommodate the regimen. At the first sign of these problems, enteral feeding should be slowed or discontinued.

Similac® Special Care® 24 with Iron Premature Infant Formula \*

Similac® Special Care® 24 Low Iron Premature Infant Formula \*\*

24 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	812
Volume, mL	124	1000
Protein, g	3	24.34
% of total calories †	12	12
Fat, g	5.43	44.07
% of total calories ††	47	47
Linoleic acid, mg	700	5681
Carbohydrate, g	10.3	83.6
% of total calories ‡	41	41
Water, g	109	885
<b>Minerals</b>		
Calcium, mg (mEq)	180 (9)	1461 (72.9)
Phosphorus, mg (mEq)	100 (3.2)	812 (26.2)
Magnesium, mg	12	97.4
Iron, mg	1.8* (0.37)**	14.6* (3)**
Zinc, mg	1.5	12.17
Manganese, mcg	12	97
Copper, mcg	250	2029
Molybdenum, mcg	—	—
Iodine, mcg	6	49
Selenium, mcg	1.8	14.6
Sodium, mg (mEq)	43 (1.9)	349 (15.2)
Potassium, mg (mEq)	129 (3.3)	1047 (26.8)
Chloride, mg (mEq)	81 (2.3)	657 (18.6)
<b>Vitamins</b>		
Vitamin A, IU	1250	10144
Vitamin D, IU	150	1217
Vitamin E, IU	4	32.5
Vitamin K, mcg	12	97.4
Thiamine (B <sub>1</sub> ), mcg	250	2029
Riboflavin (B <sub>2</sub> ), mcg	620	5032
Vitamin B <sub>6</sub> , mcg	250	2029
Vitamin B <sub>12</sub> , mcg	0.55	4.46
Niacin, mcg	5000	40578
Folic acid (Folacin), mcg	37	300
Pantothenic acid, mcg	1900	15419
Biotin, mcg	37	300
Vitamin C (Ascorbic acid), mg	37	300
Choline, mg	10	81
Inositol, mg	40	325
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	8.9	72.2
Renal Solute Load, mOsm	27.8	225.8
Osmolality, mOsm/kg H <sub>2</sub> O	280	280
Osmolarity, mOsm/L	246	246

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

\*\* Low-Iron: Additional iron should be supplied from other sources.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: Medium chain triglyceride, soy, and coconut oils (0.25% DHA; 0.4% ARA).

‡ Carbohydrate Source: Corn syrup solids and lactose.

**Precautions:** Tolerance to enteral feedings should be confirmed by initially offering small volumes of hypocaloric formula followed by cautious progression to higher caloric feedings. Spitting up, excessive gastric residuals, abdominal distention, abnormal stools or stool patterns, or other signs of intestinal dysfunction have been associated with enteral feeding before the intestinal tract is ready to accommodate the regimen. At the first sign of these problems, enteral feeding should be slowed or discontinued.

## Similac® Special Care® 30 with Iron Premature Infant Formula

30 Cal/fl oz

Available as ready-to-feed

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1014
Volume, mL	99	1000
Protein, g	3	30.4
% of total calories †	12	12
Fat, g	6.61	67.1
% of total calories ††	57	57
Linoleic acid, mg	700	7101
Carbohydrate, g	7.73	78.4
% of total calories ‡	31	31
Water, g	84	852
<b>Minerals</b>		
Calcium, mg (mEq)	180 (9)	1826 (91.3)
Phosphorus, mg (mEq)	100 (3.2)	1014 (32.4)
Magnesium, mg	12	122
Iron, mg	1.8*	18.3*
Zinc, mg	1.5	15.22
Manganese, mcg	12	122
Copper, mcg	250	2536
Molybdenum, mcg	—	—
Iodine, mcg	6	61
Selenium, mcg	1.8	18.3
Sodium, mg (mEq)	43 (1.9)	436 (19)
Potassium, mg (mEq)	129 (3.3)	1308 (33.5)
Chloride, mg (mEq)	81 (2.3)	821 (23.2)
<b>Vitamins</b>		
Vitamin A, IU	1250	12681
Vitamin D, IU	150	1522
Vitamin E, IU	4	40.6
Vitamin K, mcg	12	122
Thiamine (B <sub>1</sub> ), mcg	250	2536
Riboflavin (B <sub>2</sub> ), mcg	620	6290
Vitamin B <sub>6</sub> , mcg	250	2536
Vitamin B <sub>12</sub> , mcg	0.55	5.58
Niacin, mcg	5000	50722
Folic acid (Folacin), mcg	37	375
Pantothenic acid, mcg	1900	19274
Biotin, mcg	37	375.3
Vitamin C (Ascorbic acid), mg	37	375
Choline, mg	10	101
Inositol, mg	40	406
L-Carnitine, mg		
Taurine, mg		
Nucleotide fortification, mg		
Renal Solute Load, mOsm	27.8	282.3
Osmolality, mOsm/kg H <sub>2</sub> O	325	325
Osmolarity, mOsm/L		

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk, whey protein concentrate.

†† Fat Source: Medium chain triglycerides, soy oil, coconut oil (0.21% DHA; 0.33% ARA).

‡ Carbohydrate Source: Corn syrup solids, lactose.



### 386 **Similac® Special Care® with Iron 24 + Similac® Special Care® with Iron 30**

Similac® Special Care® with Iron 24 + Similac® Special Care® with Iron 30  
Similac® Special Care® with Iron 24 mixed with Similac® Special Care® with  
Iron 30

Nutrient per 100 mL	2:1 ratio	1:1 ratio	1:2 ratio
	26 Cal/fl oz	27 Cal/fl oz	28 Cal/fl oz
Energy, Cal	88	91	95
Protein, g	2.64	2.74	2.84
Fat, g	5.17	5.56	5.94
Carbohydrate, g	8.2	8.1	8
<b>Minerals</b>			
Calcium, mg	158	164	170
Phosphorus, mg	88	91	95
Magnesium, mg	10.6	11	11.4
Iron, mg	1.58	1.64	1.7
Zinc, mg	1.32	1.37	1.42
Manganese, mcg	11	11	11
Copper, mcg	220	228	237
Iodine, mcg	5	5	6
Sodium, mg	38	39	41
Potassium, mg	113	118	122
Chloride, mg	71	74	77
<b>Vitamins</b>			
Vitamin A, IU	1099	1141	1184
Vitamin D, IU	132	137	142
Vitamin E, IU	3.5	3.7	3.8
Vitamin K, mcg	10.6	11	11.4
Thiamine (B1), mcg	220	228	237
Riboflavin (B2), mcg	545	566	587
Vitamin B6, mcg	220	228	237
Vitamin B12, mcg	0.48	0.5	0.52
Niacin, mcg	4396	4565	4734
Folic acid (Folacin), mcg	32.5	33.8	35
Pantothenic acid, mcg	1670	1735	1799
Biotin, mcg	32.5	33.8	35
Vitamin C (Ascorbic acid), mg	33	34	35
Choline, mg	9	9	9
Inositol, mg	35	37	38
Renal Solute Load, mOsm	24.5	25.4	26.3
Approx. Osmolality, mOsm/kg H <sub>2</sub> O	295	305	310

**Similac® Special Care® 24 High Protein**

24 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	812
Volume, mL	124	1000
Protein, g	3.3	26.8
% of total calories †	13	13
Fat, g	5.43	44.1
% of total calories ††	47	47
Carbohydrate, g	10	81
% of total calories §	40	40
<b>Minerals</b>		
Calcium, mg (mEq)	180 (9)	1461 (72.9)
Phosphorus, mg (mEq)	100 (3.2)	812 (26.2)
Magnesium, mg	12	97.4
Iron, mg	1.8*	14.6*
Zinc, mg	1.5	12.2
Manganese, mcg	12	97
Copper, mcg	250	2029
Iodine, mcg	6	49
Selenium, mcg	1.8	14.6
Sodium, mg (mEq)	43 (1.9)	349 (15.2)
Potassium, mg (mEq)	129 (3.3)	1047 (26.8)
Chloride, mg (mEq)	81 (2.3)	657 (18.6)
<b>Vitamins</b>		
Vitamin A, IU	1250	10144
Vitamin D, IU	150	1217
Vitamin E, IU	4	32.5
Vitamin K, mcg	12	97.4
Thiamin B <sub>1</sub> , mcg	250	2029
Riboflavin B <sub>2</sub> , mcg	620	5032
Vitamin B <sub>6</sub> , mcg	250	2029
Vitamin B <sub>12</sub> , mcg	0.55	4.5
Niacin, mcg	5000	40578
Folic Acid, mcg	37	300
Pantothenic Acid, mcg	1900	15419
Biotin, mcg	37	300
Vitamin C, mg	37	300
Choline, mg	10	81
Inositol, mg	40	325
Linoleic Acid, mg	700	5681
Renal Solute Load, mOsm	29.5	240
Osmolality, mOsm/kg H <sub>2</sub> O	280	280

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: Medium chain triglyceride, soy, and coconut oils (0.25% DHA; 0.4% ARA).

§ Carbohydrate source: Corn syrup solids and lactose.

# 388 **Similac® Special Care® 24 High Protein + Similac® Special Care® with Iron 30**

Similac® Special Care® 24 High Protein with Iron mixed with  
Similac® Special Care® with Iron 30

Nutrient per 100 mL	2:1 ratio 26 Cal/fl oz	1:1 ratio 27 Cal/fl oz	1:2 ratio 28 Cal/fl oz
Energy, Cal	88	91	95
Volume, mL	100	100	100
Protein, g	2.8	2.86	2.92
Fat, g	5.17	5.56	5.94
Carbohydrate, g	8	8	7.9
<b>Minerals</b>			
Calcium, mg	158	164	170
Phosphorus, mg	88	91	95
Magnesium, mg	10.6	11	11.4
Iron, mg	1.58	1.64	1.7
Zinc, mg	1.32	1.37	1.42
Manganese, mcg	11	11	11
Copper, mcg	220	228	237
Iodine, mcg	5	5	6
Selenium, mcg	1.6	1.6	1.7
Sodium, mg (mEq)	38 (1.6)	39 (1.7)	41 (1.8)
Potassium, mg (mEq)	113 (2.9)	118 (3)	122 (3.1)
Chloride, mg (mEq)	71 (2)	74 (2.1)	77 (2.2)
<b>Vitamins</b>			
Vitamin A, IU	1099	1141	1184
Vitamin D, IU	132	137	142
Vitamin E, IU	3.5	3.7	3.8
Vitamin K, mcg	10.6	11	11.4
Thiamin B <sub>1</sub> , mcg	220	228	237
Riboflavin B <sub>2</sub> , mcg	545	566	587
Vitamin B <sub>6</sub> , mcg	220	228	237
Vitamin B <sub>12</sub> , mcg	0.48	0.5	0.52
Niacin, mcg	4396	4565	4734
Folic Acid, mcg	32.5	33.8	35
Pantothenic Acid, mcg	1670	1735	1799
Biotin, mcg	32.5	33.8	35
Vitamin C, mg	33	34	35
Choline, mg	9	9	9
Inositol, mg	35	37	38
Linoleic Acid, mg	615	639	663
Renal Solute Load, mOsm	25.4	26.1	26.8
Osmolality, mOsm/kg H <sub>2</sub> O	295	305	310

**Similac® Advance®**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
<b>Energy, Cal</b>	100	676
<b>Volume, mL</b>	148	1000
<b>Protein, g</b>	2.07	14
% of total calories †	8	8
<b>Fat, g</b>	5.4	36.5
% of total calories ††	49	49
<b>Linoleic acid, mg</b>	1000	6757
<b>Carbohydrate, g</b>	11.2	75.7
% of total calories ‡	43	43
<b>Water, g</b>	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	78 (3.9)	528 (26.3)
Phosphorus, mg (mEq)	42 (1.3)	284 (9.1)
Magnesium, mg	6	41
Iron, mg	1.8*	12*
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	105 (2.7)	710 (18.2)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	100	676
Riboflavin (B <sub>2</sub> ), mcg	150	1014
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.7	31.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
<b>Renal Solute Load, mOsm</b>	18.7	126.7
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	310	310
<b>Osmolarity, mOsm/L</b>	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

‡ Carbohydrate Source: Lactose and galactooligosaccharides (GOS)\*\*.

\*\* GOS (prebiotic) is approximately 5% of the total carbohydrate and provides approximately 1.3 Cal/g.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Similac® PM 60/40

20 Cal/fl oz

Available as powder.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.2	15
% of total calories †	9	9
Fat, g	5.6	37.9
% of total calories ††	50	50
Linoleic acid, mg	1000	6763
Carbohydrate, g	10.2	69
% of total calories ‡	41	41
Water, g	134	899
<b>Minerals</b>		
Calcium, mg (mEq)	56 (2.8)	379 (18.9)
Phosphorus, mg (mEq)	28 (0.9)	189 (6)
Magnesium, mg	6	40.6
Iron, mg	0.7*	4.7*
Zinc, mg	0.8	5.1
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	80 (2.1)	541 (13.8)
Chloride, mg (mEq)	59 (1.7)	399 (11.3)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	100	676
Riboflavin (B <sub>2</sub> ), mcg	150	1014
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	1.7
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	24	162
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	18.3	124.1
Osmolality, mOsm/kg H <sub>2</sub> O	280	280
Osmolarity, mOsm/L	—	—

\* Additional iron should be supplied from other sources.

† Protein Source: Whey protein concentrate and sodium caseinate.

†† Fat Source: High oleic safflower, coconut, and soy oils.

‡ Carbohydrate Source: Lactose.

**Precautions:** In conditions where the infant is losing abnormal quantities of one or more electrolytes, it may be necessary to supply electrolytes from sources other than the formula. It may be necessary to supply low-birth-weight infants (weighing less than 1500 g at birth) with additional calcium, phosphorus, and sodium during periods of rapid growth.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Similac Sensitive® (Formerly Similac® Lactose Free)**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.14	14.47
% of total calories †	9	9
Fat, g	5.4	36.52
% of total calories ††	49	49
Linoleic acid, mg	1000	6763
Carbohydrate, g	11.1	75.1
% of total calories ‡	43	43
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	84 (4.2)	568 (28.3)
Phosphorus, mg (mEq)	56	379
Magnesium, mg	6	40.6
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	9	61
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	30 (1.3)	203 (8.8)
Potassium, mg (mEq)	107 (2.7)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	3	20.3
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	100	676
Riboflavin (B <sub>2</sub> ), mcg	150	1014
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.3	29.1
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	19.9	134.7
Osmolality, mOsm/kg H <sub>2</sub> O	200	200
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Milk protein isolate.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

‡ Carbohydrate Source: Corn maltodextrin and sucrose.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Similac Sensitive® for Spit-Up™ (formerly Similac Sensitive® R.S.)

20 Cal/fl oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories †	9	9
Fat, g	5.4	36.5
% of total calories ††	49	49
Linoleic acid, mg	1000	6760
Carbohydrate, g	10.7	72.4
% of total calories ‡	43	43
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	84 (4.2)	568 (28.3)
Phosphorus, mg (mEq)	56 (1.8)	379 (12.2)
Magnesium, mg	6	40.6
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.1
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	90	609
Iodine, mcg	9	61
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	30 (1.3)	203 (8.8)
Potassium, mg (mEq)	107 (2.7)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	3	20.3
Vitamin K, mcg	8	54
Thiamin B <sub>1</sub> , mcg	100	676
Riboflavin B <sub>2</sub> , mcg	150	1014
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.25	1.7
Niacin, mcg	1050	7101
Folic acid, mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C, mg	9	61
Choline, mg	16	108
Inositol, mg	4.3	29.1
Carnitine, mg	4.3	29.1
Taurine, mg	4.3	29.1
Nucleotide fortification, mg	4.3	29.1
Renal Solute Load, mOsm	19.9	134.7
Osmolality, mOsm/kg H <sub>2</sub> O	200	200
Osmolarity, mOsm/L	180	180

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Milk protein isolate.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

‡ Carbohydrate source: Corn syrup, rice starch, and sugar.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Similac® Organic**

20 Cal/fl oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.07	14
% of total calories †	8	8
Fat, g	5.49	37.1
% of total calories ††	49	49
Linoleic acid, mg	860	5816
Carbohydrate, g	10.56	71.4
% of total calories ‡	42	42
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	78 (3.9)	528 (26.3)
Phosphorus, mg (mEq)	42 (1.3)	284 (9.1)
Magnesium, mg	6	41
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	105 (2.7)	710 (18.1)
Chloride, mg (mEq)	65 (1.8)	439 (12.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	100	676
Riboflavin (B <sub>2</sub> ), mcg	150	1014
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.7	31.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	**	**
Renal Solute Load, mOsm	18.8	126.8
Osmolality, mOsm/kg H <sub>2</sub> O	225	225
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Organic nonfat dry milk.

†† Fat Source: Organic high oleic sunflower, organic soy, and organic coconut oils (0.15% DHA; 0.4% ARA).

‡ Carbohydrate Source: Organic corn maltodextrin, organic lactose, and organic sugar from evaporated cane juice.

\*\* Contains C. Cohnii oil, a source of docosahexaenoic acid (DHA), and M. Alpina oil, a source of arachidonic acid (ARA).

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.



**Nutritionally Complete Amino Acid-Based Medical Food and Infant Formula with Iron \***

20 Cal/fl oz

Available as powder.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3.1	20.6
% of total calories †	15	15
Fat, g	4.8	32.7
% of total calories ††	42	42
Linoleic acid, mg	840	5680
Carbohydrate, g	10.7	72.4
% of total calories §	43	43
Water, g	132.5	895
<b>Minerals</b>		
Calcium, mg (mEq)	116 (5.8)	781 (39.2)
Phosphorus, mg (mEq)	84.2 (2.7)	568 (18.2)
Magnesium, mg	8.4	56.8
Iron, mg	1.5*	9.9*
Zinc, mg	0.8	5.7
Manganese, mcg	84	568
Copper, mcg	105	710
Molybdenum, mcg	2.5	17.1
Iodine, mcg	8.4	57
Selenium, mcg	2.3	15.6
Sodium, mg (mEq)	45 (2)	305 (13.3)
Potassium, mg (mEq)	150 (3.9)	1015 (26)
Chloride, mg (mEq)	60 (1.7)	405 (11.4)
<b>Vitamins</b>		
Vitamin A, IU	273	1846
Vitamin D, IU	60	406
Vitamin E, IU	2.1	14.2
Vitamin K, mcg	6	40.5
Thiamine (B <sub>1</sub> ), mcg	210	1420
Riboflavin (B <sub>2</sub> ), mcg	105	710
Vitamin B <sub>6</sub> , mcg	84.2	568
Vitamin B <sub>12</sub> , mcg	0.4	2.8
Niacin, mcg	1680	11400
Folic acid (Folacin), mcg	29.5	199
Pantothenic acid, mcg	421	2840
Biotin, mcg	4.2	28.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	9.5	64
Inositol, mg	5.1	34
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	28	187
Osmolality, mOsm/kg H <sub>2</sub> O	350	350
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Free L-amino acids.

†† Fat Source: High oleic safflower, medium chain triglyceride, and soy oils.

§ Carbohydrate Source: Corn syrup solids.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Dilution Table - EleCare® Powder

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked Scoopful	Approximate Yield (fl oz)
20*	2	1	2
22	3.5	2	4
24	8	5	9
27	7	5	8
30**	5	4	6

\* Standard infant mixture.

\*\* Standard pediatric mixture.

## Similac® Soy Isomil®

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.45	16.57
% of total calories †	10	10
Fat, g	5.46	36.93
% of total calories ††	49	49
Linoleic acid, mg	1000	6763
Carbohydrate, g	10.4	69.7
% of total calories §	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	105 (5.2)	710 (35.4)
Phosphorus, mg (mEq)	75 (2.4)	507 (16.4)
Magnesium, mg	7.5	50.7
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.07
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	44 (1.9)	298 (12.9)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	62 (1.8)	419 (11.8)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	11	74
Thiamine (B <sub>1</sub> ), mcg	60	406
Riboflavin (B <sub>2</sub> ), mcg	90	609
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.45	3.04
Niacin, mcg	1350	9130
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	750	5072
Biotin, mcg	4.5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	5	33.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	22.8	154.5
Osmolality, mOsm/kg H <sub>2</sub> O	200	200
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Soy protein isolate and L-methionine.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

§ Carbohydrate Source: Corn syrup, sugar, and prebiotic fructooligosaccharides (FOS).

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Similac Expert Care™ 24 Cal with Iron

24 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	806
Volume, mL	124	1000
Protein, g	2.7	21.8
% of total calories †	11	11
Fat, g	5.3	42.7
% of total calories ††	47	47
Linoleic acid, mg	1300	10483
Carbohydrate, g	10.5	84.7
% of total calories ‡	42	42
Water, g	109	879
<b>Minerals</b>		
Calcium, mg (mEq)	90 (4.5)	726 (36.3)
Phosphorus, mg (mEq)	70 (2.3)	565 (18.6)
Magnesium, mg	7	56.5
Iron, mg	1.8*	14.5*
Zinc, mg	0.75	6
Manganese, mcg	5	40.3
Copper, mcg	90	726
Molybdenum, mcg	—	—
Iodine, mcg	9	72.6
Selenium, mcg	1.8	14.5
Sodium, mg (mEq)	32 (1.4)	258 (11.3)
Potassium, mg (mEq)	132 (3.4)	1065 (27.4)
Chloride, mg (mEq)	81 (2.3)	653 (18.5)
<b>Vitamins</b>		
Vitamin A, IU	300	2419
Vitamin D, IU	60	484
Vitamin E, IU	1.5	12.1
Vitamin K, mcg	8	64.5
Thiamin B <sub>1</sub> , mcg	100	806
Riboflavin B <sub>2</sub> , mcg	150	1210
Vitamin B <sub>6</sub> , mcg	60	484
Vitamin B <sub>12</sub> , mcg	0.25	2
Niacin, mcg	1050	8468
Folic Acid, mcg	15	121
Pantothenic Acid, mcg	450	3629
Biotin, mcg	4.4	35.5
Vitamin C, mg	9	72.6
Choline, mg	16	129
Inositol, mg	4.7	37.9
Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	—	—
Osmolality, mOsm/kg H <sub>2</sub> O	280	280
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk.

†† Fat Source: Soy and coconut oils.

‡ Carbohydrate source: Lactose.

## Similac® Expert Care™ Alimentum® Hypoallergenic Formula

20 Cal/fl oz

Available as powder (P) and ready-to-feed (L).

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.75	18.6
% of total calories †	11	11
Fat, g	5.54	37.47
% of total calories ††	48	48
Linoleic acid, mg	800 (P) 1900 (L)	5405 (P) 12850 (L)
Carbohydrate, g	10.2	69
% of total calories ‡	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	105 (5.2)	710 (35.4)
Phosphorus, mg (mEq)	75 (2.4)	507 (16.4)
Magnesium, mg	7.5	50.7
Iron, mg	1.8*	12.17*
Zinc, mg	0.75	5.07
Manganese, mcg	8	54
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	44 (1.9)	298 (12.9)
Potassium, mg (mEq)	118 (3)	798 (20.3)
Chloride, mg (mEq)	80 (2.3)	541 (15.2)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	45	304
Vitamin E, IU	3	20.3
Vitamin K, mcg	8 (P) 15 (L)	54 (P) 101 (L)
Thiamine (B <sub>1</sub> ), mcg	60	406
Riboflavin (B <sub>2</sub> ), mcg	90	609
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.45	3.04
Niacin, mcg	1350	9130
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	750	5072
Biotin, mcg	4.5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	5	33.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25.3	171.3
Osmolality, mOsm/kg H <sub>2</sub> O	320 (P) 370 (L)	320 (P) 370 (L)
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate, L-cystine, L-tyrosine, and L-tryptophan.

†† Fat Source: High-oleic safflower, medium chain triglyceride, and soy oils (0.15% DHA; 0.4% ARA).

‡ Carbohydrate Source: Powder, corn maltodextrin and sugar (sucrose); Liquid, sugar and modified tapioca starch.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Similac Expert Care™ for Diarrhea

20 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.66	17.99
% of total calories †	11	11
Fat, g	5.46	36.93
% of total calories ††	49	49
Linoleic acid, mg	1300	8792
Carbohydrate, g	10.1	68.3
% of total calories ‡	40	40
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	105 (5.2)	710 (35.4)
Phosphorus, mg (mEq)	75 (2.4)	507 (16.2)
Magnesium, mg	7.5	50.7
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.1
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	44 (1.9)	298 (12.9)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	62 (1.8)	419 (11.8)
<b>Vitamins</b>		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	11	74
Thiamin B <sub>1</sub> , mcg	60	406
Riboflavin B <sub>2</sub> , mcg	90	609
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.45	3.04
Niacin, mcg	1350	9130
Folic Acid, mcg	15	101
Pantothenic Acid, mcg	750	5072
Biotin, mcg	4.5	30.4
Vitamin C, mg	9	61
Choline, mg	12	81
Inositol, mg	5	33.8
Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	24	162.6
Osmolality, mOsm/kg H <sub>2</sub> O	240	240
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Soy protein isolate.

†† Fat Source: Soy and coconut oils.

‡ Carbohydrate source: Corn syrup solids and sugar.

## Similac® Expert Care™ NeoSure®

22 Cal/fl oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	744
Volume, mL	134	1000
Protein, g	2.8	20.83
% of total calories †	11	11
Fat, g	5.5	40.92
% of total calories ††	49	49
Linoleic acid, mg	750	5579
Carbohydrate, g	10.1	75.1
% of total calories ‡	40	40
Water, g	120	893
<b>Minerals</b>		
Calcium, mg (mEq)	105 (5.2)	781 (39)
Phosphorus, mg (mEq)	62 (2)	461 (14.9)
Magnesium, mg	9	67
Iron, mg	1.8*	13.4*
Zinc, mg	1.2	8.9
Manganese, mcg	10	74
Copper, mcg	120	893
Molybdenum, mcg	—	—
Iodine, mcg	15	112
Selenium, mcg	2.3	17.1
Sodium, mg (mEq)	33 (1.4)	245 (10.7)
Potassium, mg (mEq)	142 (3.6)	1056 (27)
Chloride, mg (mEq)	75 (2.1)	558 (15.7)
<b>Vitamins</b>		
Vitamin A, IU	350	2604
Vitamin D, IU	70	521
Vitamin E, IU	3.6	26.8
Vitamin K, mcg	11	81.8
Thiamine (B <sub>1</sub> ), mcg	175	1302
Riboflavin (B <sub>2</sub> ), mcg	150	1116
Vitamin B <sub>6</sub> , mcg	100	744
Vitamin B <sub>12</sub> , mcg	0.4	2.98
Niacin, mcg	1950	14506
Folic acid (Folacin), mcg	25	186
Pantothenic acid, mcg	800	5951
Biotin, mcg	9	67
Vitamin C (Ascorbic acid), mg	15	112
Choline, mg	16	119
Inositol, mg	35	260
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25.2	187.4
Osmolality, mOsm/kg H <sub>2</sub> O	250	250
Osmolarity, mOsm/L	—	—

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: Soy, coconut high oleic safflower, and medium chain triglyceride oils (0.25% DHA; 0.4% ARA).

‡ Carbohydrate Source: Corn syrup solids and lactose.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**PediaSure® Complete, Balanced Nutrition®**  
 30 Cal/fl oz (Ready to Use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1000
Volume, mL	100	1000
Protein, g	3	30
% of total calories †	12	12
Fat, g	3.8	38
% of total calories ††	35	35
Linoleic acid, mg	—	—
Carbohydrate, g	13.1	131
% of total calories ‡	53	53
Water, g	84.5	845
<b>Minerals</b>		
Calcium, mg (mEq)	97.2 (4.9)	972 (49)
Phosphorus, mg (mEq)	84.5 (2.7)	845 (27)
Magnesium, mg	19.9	199
Iron, mg	1.4	14
Zinc, mg	0.59	5.9
Manganese, mcg	150	1500
Copper, mcg	100	1000
Molybdenum, mcg	3.6	36
Iodine, mcg	9.7	97
Selenium, mcg	3.2	32
Sodium, mg (mEq)	38 (1.7)	380 (17)
Potassium, mg (mEq)	131 (3.4)	1310 (34)
Chloride, mg (mEq)	101.4 (2.9)	1014 (29)
<b>Vitamins</b>		
Vitamin A, IU	160.6	1606
Vitamin D, IU	51	507
Vitamin E, IU	2.3	23
Vitamin K, mcg	5.9	59
Thiamine (B <sub>1</sub> ), mcg	270	2700
Riboflavin (B <sub>2</sub> ), mcg	210	2100
Vitamin B <sub>6</sub> , mcg	260	2600
Vitamin B <sub>12</sub> , mcg	0.59	5.9
Niacin, mcg	1000	10000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	1000	10000
Biotin, mcg	19	190
Vitamin C (Ascorbic acid), mg	10.1	101
Choline, mg	30	300
Inositol, mg	8	80
L-Carnitine, mg	1.7	17
Taurine, mg	7.2	72
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27.5	275
Osmolality, mOsm/kg H <sub>2</sub> O*	480	480
Osmolarity, mOsm/L	364	364

† Protein Source: Milk protein concentrate, whey protein concentrate, and soy protein isolate

†† Fat Source: High-oleic safflower, soy and medium chain triglyceride oils

‡ Carbohydrate Source: Sucrose and corn maltodextrin

\* Vanilla, strawberry, banana cream; chocolate = 540 mOsm/kg water; orange cream = 560 mOsm/kg water.

Chocolate PediaSure® does not contain whey protein concentrate.

**Precaution:** Not for children with galactosemia.



**PediaSure® Enteral**  
**Complete, Balanced Nutrition®**  
 30 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1000
Volume, mL	100	1000
Protein, g	3	30
% of total calories †	12	12
Fat, g	4	40
% of total calories ††	35	35
Linoleic acid, mg	—	—
Carbohydrate, g	13.3	133
% of total calories ‡	53	53
Water, g	85.4	854
<b>Minerals</b>		
Calcium, mg (mEq)	97.2 (4.9)	972 (49)
Phosphorus, mg (mEq)	84.5 (2.7)	845 (27)
Magnesium, mg	19.9	199
Iron, mg	1.4	14
Zinc, mg	0.59	5.9
Manganese, mcg	150	1500
Copper, mcg	100	1000
Molybdenum, mcg	3.6	36
Iodine, mcg	9.7	97
Selenium, mcg	3.2	32
Sodium, mg (mEq)	38 (1.7)	380 (17)
Potassium, mg (mEq)	131 (3.4)	1310 (34)
Chloride, mg (mEq)	101.4 (2.9)	1014 (29)
<b>Vitamins</b>		
Vitamin A, IU	160.6	1606
Vitamin D, IU	50.7	507
Vitamin E, IU	2.3	23
Vitamin K, mcg	5.9	59
Thiamine (B <sub>1</sub> ), mcg	270	2700
Riboflavin (B <sub>2</sub> ), mcg	210	2100
Vitamin B <sub>6</sub> , mcg	260	2600
Vitamin B <sub>12</sub> , mcg	0.59	5.9
Niacin, mcg	1000	10000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	1000	10000
Biotin, mcg	19	190
Vitamin C (Ascorbic acid), mg	10.1	101
Choline, mg	30	300
Inositol, mg	8	80
L-Carnitine, mg	1.7	17
Taurine, mg	7.2	72
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27.7	277
Osmolality, mOsm/kg H <sub>2</sub> O	335	335
Osmolarity, mOsm/L	—	—

† Protein Source: Milk protein concentrate.

†† Fat Source: High oleic safflower, soy, and medium chain triglyceride oils.

‡ Carbohydrate Source: Sucrose and corn maltodextrin.

Kosher. Gluten-free. Lactose-free.

**Precaution:** Not for children with galactosemia.

**Enfamil® EnfaCare®**

22 Cal/fl oz

Available as powder (P) and ready-to-feed (L).

Nutrient	per 100 Cal	per Liter
<b>Energy, Cal</b>	100	746
<b>Volume, mL</b>	134	1000
<b>Protein, g</b>	2.8	20.8
% of total calories †	11	11
<b>Fat, g</b>	5.3	39.5
% of total calories ††	47	47
Linoleic acid, mg	950	7087
<b>Carbohydrate, g</b>	10.4	77.6
% of total calories ‡	42	42
<b>Water, g</b>	117 (P) 120 (L)	873 (P) 895 (L)
<b>Minerals</b>		
Calcium, mg (mEq)	120 (6)	895 (44.8)
Phosphorus, mg (mEq)	66 (2.1)	492 (15.7)
Magnesium, mg	8	60
Iron, mg	1.8*	13.4*
Zinc, mg	1 (P) 1.25 (L)	7.5 (P) 9.3 (L)
Manganese, mcg	15	112
Copper, mcg	120	895
Molybdenum, mcg	—	—
Iodine, mcg	21	156
Selenium, mcg	2.8	20.8
Sodium, mg (mEq)	37 (1.6) (P)	276 (12) (P)
	35 (1.5) (L)	261 (11.3) (L)
Potassium, mg (mEq)	105 (2.7)	783 (20)
Chloride, mg (mEq)	78 (2.2)	581 (16.4)
<b>Vitamins</b>		
Vitamin A, IU	450	3357
Vitamin D, IU	70	522
Vitamin E, IU	4	30
Vitamin K, mcg	8	60
Thiamine (B <sub>1</sub> ), mcg	200	1492
Riboflavin (B <sub>2</sub> ), mcg	200	1492
Vitamin B <sub>6</sub> , mcg	60 (P) 100 (L)	448 (P) 746 (L)
Vitamin B <sub>12</sub> , mcg	0.3	2.2
Niacin, mcg	1000 (P) 2000 (L)	7463 (P) 14920 (L)
Folic acid (Folacin), mcg	26	194
Pantothenic acid, mcg	850	6341
Biotin, mcg	5 (P) 6 (L)	37 (P) 45 (L)
Vitamin C (Ascorbic acid), mg	16	119
Choline, mg	24	179
Inositol, mg	30	224
L-Carnitine, mg	2	14.9
Taurine, mg	6	45
Nucleotide fortification, mg	4	31
<b>Renal Solute Load, mOsm</b>	25	184 (P) 183 (L)
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	310 (P) 250 (L)	310 (P) 250 (L)
<b>Osmolarity, mOsm/L</b>	270 (P) 220 (L)	270 (P) 220 (L)

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

†† Fat Source: High-oleic vegetable 34%, soy 29%, and medium chain triglyceride 20%, coconut oils 14%, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Powder: lactose 70% and corn syrup solids 30% Liquid: Maltodextrin 60%, lactose 40%.

(P) Powder; (L) Liquid

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

# **Enfamil® EnfaCare® + Enfamil® LIPIL® Concentrate 24**

**Enfamil® EnfaCare® + Enfamil® LIPIL® Concentrate 24**  
24 Cal/11 oz (see footnotes for preparation)

<b>Nutrient</b>	<b>per 100 Cal</b>	<b>per Liter</b>
<b>Energy, Cal</b>	100	813
<b>Volume, mL</b>	123	1000
<b>Protein, g</b>	2.7	22
% of total calories †	10.8	10.8
<b>Fat, g</b>	5.3	43
% of total calories ††	47.2	47.2
<b>Linoleic acid, mg</b>	932	7611
<b>Carbohydrate, g</b>	10.5	85
% of total calories ‡	42	42
<b>Water, g</b>	108	883
<b>Minerals</b>		
Calcium, mg (mEq)	116 (5.9)	940 (47)
Phosphorus, mg (mEq)	64 (2.1)	520 (17)
Magnesium, mg	8	65
Iron, mg	1.8	14.6
Zinc, mg	1.23	10
Manganese, mcg	15	122
Copper, mcg	116	940
Molybdenum, mcg	—	—
Iodine, mcg	20	162
Selenium, mcg	2.8	23
Sodium, mg (mEq)	34 (1.5)	280 (12.2)
Potassium, mg (mEq)	105 (2.7)	850 (21.8)
Chloride, mg (mEq)	77 (2.2)	620 (17.5)
<b>Vitamins</b>		
Vitamin A, IU	440	3600
Vitamin D, IU	78	630
Vitamin E, IU	3.8	31
Vitamin K, mcg	8	65
Thiamine (B <sub>1</sub> ), mcg	188	1530
Riboflavin (B <sub>2</sub> ), mcg	194	1570
Vitamin B <sub>6</sub> , mcg	96	780
Vitamin B <sub>12</sub> , mcg	0.3	2.4
Niacin, mcg	1900	15400
Folic acid (Folacin), mcg	25	200
Pantothenic acid, mcg	820	6700
Biotin, mcg	5.7	46
Vitamin C (Ascorbic acid), mg	15.6	127
Choline, mg	24	195
Inositol, mg	28	230
L-Carnitine, mg	2	16.2
Taurine, mg	6	49
Nucleotide fortification, mg	4.2	34
<b>Renal Solute Load, mOsm</b>	23.9	193.9
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	255	255
<b>Osmolarity, mOsm/L</b>	226	226

† Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

†† Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Maltodextrin 60%, lactose 40%.

**Preparation:** Enfamil EnfaCare 3 fl oz Nursette + 12 mL Enfamil Lipil liquid concentrate (provides volume based dilution 90% Enfamil EnfaCare + 10% Enfamil Lipil liquid concentrate).

# **Enfamil® EnfaCare® + Enfamil® LIPIL® Concentrate 27**

405

**Enfamil® EnfaCare® + Enfamil® LIPIL® Concentrate 27**  
27 Cal/11 oz (see footnotes for preparation)

<b>Nutrient</b>	<b>per 100 Cal</b>	<b>per Liter</b>
<b>Energy, Cal</b>	100	878
<b>Volume, mL</b>	114	1000
<b>Protein, g</b>	2.6	24
% of total calories †	10.4	10.4
<b>Fat, g</b>	5.3	48
% of total calories ††	47.2	47.2
<b>Linoleic acid, mg</b>	920	8071
<b>Carbohydrate, g</b>	10.6	97
% of total calories ‡	42.4	42.4
<b>Water, g</b>	100	875
<b>Minerals</b>		
Calcium, mg (mEq)	107 (5.4)	963 (48)
Phosphorus, mg (mEq)	59 (1.9)	531 (17.1)
Magnesium, mg	8	73
Iron, mg	1.8	16.4
Zinc, mg	1.18	10.8
Manganese, mcg	15	137
Copper, mcg	107	963
Molybdenum, mcg	—	—
Iodine, mcg	17.7	152
Selenium, mcg	2.8	26
Sodium, mg (mEq)	33 (1.4)	297 (12.9)
Potassium, mg (mEq)	106 (2.7)	931 (23.8)
Chloride, mg (mEq)	74 (2.1)	666 (18.8)
<b>Vitamins</b>		
Vitamin A, IU	410	3700
Vitamin D, IU	74	680
Vitamin E, IU	3.4	31
Vitamin K, mcg	8	73
Thiamine (B <sub>1</sub> ), mcg	164	1500
Riboflavin (B <sub>2</sub> ), mcg	182	1660
Vitamin B <sub>6</sub> , mcg	88	800
Vitamin B <sub>12</sub> , mcg	0.3	2.7
Niacin, mcg	1700	15500
Folic acid (Folacin), mcg	23	210
Pantothenic acid, mcg	750	6800
Biotin, mcg	5.1	47
Vitamin C (Ascorbic acid), mg	14.8	135
Choline, mg	24	220
Inositol, mg	23	210
L-Carnitine, mg	2	18.3
Taurine, mg	6	55
Nucleotide fortification, mg	4.2	38
<b>Renal Solute Load, mOsm</b>	22.7	199.2
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	260	260
<b>Osmolarity, mOsm/L</b>	228	228

† Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

†† Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Maltodextrin 60%, lactose 40%.

**Preparation:** Enfamil EnfaCare 3 fl oz Nursette + 35 mL Enfamil Lipil liquid concentrate (provides volume based dilution 70% Enfamil EnfaCare + 30% Enfamil Lipil liquid concentrate).

NUTRITIONALS

# **Enfamil® Premature 24 + Enfamil® LIPIL® Concentrate 30**

Enfamil® Premature 24 + Enfamil® LIPIL® Concentrate 30  
30 Cal/fl oz (see footnotes for preparation)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1030
Volume, mL	97	1000
Protein, g	2.6	26
% of total calories †	10.4	10.4
Fat, g	5.2	53
% of total calories ††	46.8	47
Linoleic acid, mg	836	8614
Carbohydrate, g	11	112
% of total calories ‡	42.8	43
Water, g	122	1250
<b>Minerals</b>		
Calcium, mg (mEq)	130 (6.4)	1320 (66)
Phosphorus, mg (mEq)	67 (2.2)	680 (22.3)
Magnesium, mg	8.6	87
Iron, mg	1.8	18.3
Zinc, mg	1.3	13.2
Manganese, mcg	9.8	99
Copper, mcg	102	1030
Molybdenum, mcg	0.24	2.4
Iodine, mcg	19	193
Selenium, mcg	2.8	28
Sodium, mg (mEq)	46 (2)	470 (20.4)
Potassium, mg (mEq)	102 (2.6)	1030 (26.4)
Chloride, mg (mEq)	79 (2.2)	814 (22.9)
<b>Vitamins</b>		
Vitamin A, IU	870	8800
Vitamin D, IU	168	1700
Vitamin E, IU	4.6	47
Vitamin K, mcg	8	81
Thiamine (B <sub>1</sub> ), mcg	152	1540
Riboflavin (B <sub>2</sub> ), mcg	240	2400
Vitamin B <sub>6</sub> , mcg	114	1160
Vitamin B <sub>12</sub> , mcg	0.27	2.7
Niacin, mcg	2800	28000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	920	9300
Biotin, mcg	3.6	37
Vitamin C (Ascorbic acid), mg	16.8	170
Choline, mg	22	220
Inositol, mg	29	290
L-Carnitine, mg	2.2	22
Taurine, mg	6	61
Nucleotide fortification, mg	4.2	43
Renal Solute Load, mOsm	23	235.8
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	255	255

† Protein Source: Whey protein concentrate 60%, nonfat milk 40%

†† Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Maltodextrin 60%, lactose 40%.

**Preparation:** Enfamil Premature 24 with iron 3 fl oz Nursette + 60 mL Enfamil Lipil liquid concentrate (provides volume based dilution 60% Enfamil Premature + 40% Enfamil Lipil liquid concentrate).

Enfamil® Premature 20 with Iron \*

Enfamil® Premature 20 low Iron \*\*

20 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3	20.3
% of total calories †	12	12
Fat, g	5.1	34.5
% of total calories ††	44	44
Linoleic acid, mg	810	5476
Carbohydrate, g	11	74.4
% of total calories ‡	44	44
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	165 (8.2)	1115 (55.8)
Phosphorus, mg (mEq)	83 (2.7)	561 (18)
Magnesium, mg	9	61
Iron, mg	1.8* (0.5)**	12.2* (3.4)**
Zinc, mg	1.5	10.1
Manganese, mcg	6.3	43
Copper, mcg	120	811
Molybdenum, mcg	0.4	2.7
Iodine, mcg	25	169
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	58 (2.5)	392 (16.9)
Potassium, mg (mEq)	98 (2.5)	662 (17)
Chloride, mg (mEq)	90 (2.5)	608 (17.1)
<b>Vitamins</b>		
Vitamin A, IU	1250	8450
Vitamin D, IU	240	1622
Vitamin E, IU	6.3	43
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	200	1352
Riboflavin (B <sub>2</sub> ), mcg	300	2028
Vitamin B <sub>6</sub> , mcg	150	1014
Vitamin B <sub>12</sub> , mcg	0.25	1.69
Niacin, mcg	4000	27040
Folic acid (Folacin), mcg	40	270
Pantothenic acid, mcg	1200	8112
Biotin, mcg	4	27
Vitamin C (Ascorbic acid), mg	20	135
Choline, mg	20	135
Inositol, mg	44	297
L-Carnitine, mg	2.4	16.2
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27	184
Osmolality, mOsm/kg H <sub>2</sub> O	240	240
Osmolarity, mOsm/L	220	220

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

\*\* Supplemental vitamin E and iron (when using low iron) should also be considered.

† Protein Source: Whey protein concentrate and nonfat milk.

†† Fat Source: Medium chain triglyceride, soy, and high-oleic vegetable oils, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Corn syrup solids and lactose.

Enfamil® Premature 24 with Iron\*

Enfamil® Premature 24 low Iron\*\*

24 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	813
Volume, mL	123	1000
Protein, g	3	24.4
% of total calories †	12	12
Fat, g	5.1	41.5
% of total calories ††	44	44
Linoleic acid, mg	810	6585
Carbohydrate, g	11	89.4
% of total calories §	44	44
Water, g	108	878
<b>Minerals</b>		
Calcium, mg (mEq)	165 (8.2)	1341 (67)
Phosphorus, mg (mEq)	83 (2.7)	674 (21.6)
Magnesium, mg	9	73
Iron, mg	1.8* (0.5)**	14.6* (4.1)**
Zinc, mg	1.5	12.2
Manganese, mcg	6.3	51
Copper, mcg	120	976
Molybdenum, mcg	0.4	3.2
Iodine, mcg	25	203
Selenium, mcg	2.8	22.8
Sodium, mg (mEq)	58 (2.5)	471 (20.5)
Potassium, mg (mEq)	98 (2.5)	797 (20.4)
Chloride, mg (mEq)	90 (2.5)	732 (20.6)
<b>Vitamins</b>		
Vitamin A, IU	1250	10163
Vitamin D, IU	240	1951
Vitamin E, IU	6.3	51
Vitamin K, mcg	8	65
Thiamine (B <sub>1</sub> ), mcg	200	1626
Riboflavin (B <sub>2</sub> ), mcg	300	2439
Vitamin B <sub>6</sub> , mcg	150	1220
Vitamin B <sub>12</sub> , mcg	0.25	2.03
Niacin, mcg	4000	32520
Folic acid (Folacin), mcg	40	325
Pantothenic acid, mcg	1200	9756
Biotin, mcg	4	32
Vitamin C (Ascorbic acid), mg	20	163
Choline, mg	20	163
Inositol, mg	44	358
L-Carnitine, mg	2.4	19.5
Taurine, mg	6	49
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27	220
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	260	260

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

\*\* Supplemental vitamin E and iron (when using Low Iron) should also be considered.

† Protein Source: Whey protein concentrate and nonfat milk.

†† Fat Source: Medium chain triglyceride, soy, and high oleic vegetable oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and lactose.

**Enfamil LIPIL®**

20 Cal/11 oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories †	8.5	8.5
Fat, g	5.3	35.8
% of total calories ††	48	48
Linoleic acid, mg	860	5811
Carbohydrate, g	10.9	73.6
% of total calories ‡	43.5	43.5
Water, g	134	905
<b>Minerals</b>		
Calcium, mg (mEq)	78 (3.9)	527 (26.4)
Phosphorus, mg (mEq)	43 (1.4)	291 (9.5)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	10	67.6
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	27 (1.2)	182 (8.1)
Potassium, mg (mEq)	108 (2.8)	730 (18.9)
Chloride, mg (mEq)	63 (1.8)	426 (12.2)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	60	405
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6757
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3378
Biotin, mcg	3	20.3
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	40.5
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Nucleotide fortification, mg	4.2	28
Renal Solute Load, mOsm	18.9	128
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	270	270

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Whey and nonfat milk.

†† Fat Source: Palm olein, soy, coconut and high-oleic sunflower oils, and single-cell oil blend (0.32% DHA; 0.64% ARA).

‡ Carbohydrate Source: Lactose from cow's milk.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.



**Enfamil A.R.®**

20 Cal/11 oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.5	16.9
% of total calories †	10	10
Fat, g	5.1	34.5
% of total calories ††	46	46
Linoleic acid, mg	860	5814
Carbohydrate, g	11	74.4
% of total calories ‡	44	44
Water, g	134	906
<b>Minerals</b>		
Calcium, mg (mEq)	78 (3.9)	527 (26.3)
Phosphorus, mg (mEq)	53 (1.7)	358 (11.5)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	10	68
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	40 (1.7)	270 (11.7)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	75 (2.1)	507 (14.3)
<b>Vitamins</b>		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	2.03
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	23	150
Osmolality, mOsm/kg H <sub>2</sub> O	240	240
Osmolarity, mOsm/L	220	220

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk

†† Fat Source: Palm olein, soy, coconut, and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Lactose, rice starch, and maltodextrin.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Enfamil® ProSobee®**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.5	16.9
% of total calories †	10	10
Fat, g	5.3	35.8
% of total calories ††	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.6	71.7
% of total calories §	42	42
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	105 (5.2)	710 (35.5)
Phosphorus, mg (mEq)	69 (2.2)	466 (14.9)
Magnesium, mg	11	74
Iron, mg	1.8*	12.2*
Zinc, mg	1.2	8.1
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	36 (1.6)	243 (10.6)
Potassium, mg (mEq)	120 (3.1)	811 (20.8)
Chloride, mg (mEq)	80 (2.3)	541 (15.2)
<b>Vitamins</b>		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	90	608
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	23	156
Osmolality, mOsm/kg H <sub>2</sub> O	170	170
Osmolarity, mOsm/L	153	153

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Soy protein isolate

†† Fat Source: Palm olein, soy, coconut, and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids.

**Potential Allergens:** Contains soy protein.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Enfamil PREMIUM® Newborn

20 Cal/fl oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories †	8.5	8.5
Fat, g	5.3	35.8
% of total calories ††	48	48
Linoleic acid, mg	860	5811
Linolenic acid, mg	80	540
Carbohydrate, g	11.2	75.7
% of total calories ‡	43.5	43.5
Water, g	133	899
<b>Minerals</b>		
Calcium, mg	78 (3.9)	527 (26.4)
Phosphorus, mg	43 (1.4)	291 (9.5)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	27 (1.2)	182 (8.1)
Potassium, mg (mEq)	108 (2.8)	730 (18.9)
Chloride, mg (mEq)	63 (1.8)	426 (12.2)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	75	507
Vitamin E, IU	2	13.5
Vitamin K, mcg	9	60.8
Thiamin B <sub>1</sub> , mcg	80	541
Riboflavin B <sub>2</sub> , mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6757
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20.3
Vitamin C, mg	12	81.1
Choline, mg	24	162
Inositol, mg	6	40.5
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Renal Solute Load, mOsm	19.1	129
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	270	270

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Whey and nonfat milk.

†† Fat Source: Palm olein oil, soy oil, coconut oil, high-oleic sunflower oil, and single-cell oils (0.32% DHA; 0.64% ARA).

‡ Carbohydrate source: Lactose from cow's milk. Also contains the prebiotic carbohydrates galactooligosaccharide and polydextrose.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Enfamil PREMIUM® Infant**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories *	8.5	8.5
Fat, g	5.3	35.9
% of total calories **	48	48
Linoleic acid, mg	860	5811
Linolenic acid, mg	80	540
Carbohydrate, g	11	74.3
% of total calories †	43.5	43.5
Water, g	133	899
<b>Minerals</b>		
Calcium, mg	78 (3.9)	527 (26.4)
Phosphorus, mg	43 (1.4)	291 (9.4)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	27 (1.2)	182 (7.9)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	63 (1.8)	426 (12)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	60	405
Vitamin E, IU	2	13.5
Vitamin K, mcg	9	60.8
Thiamine B <sub>1</sub> , mcg	80	540
Riboflavin B <sub>2</sub> , mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6757
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20.3
Vitamin C, mg	12	81
Choline, mg	24	162
Inositol, mg	6	40.5
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Renal Solute Load, mOsm	19.1	129
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	270	270

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Whey and nonfat milk.

\*\* Fat Source: Palm olein oil, soy oil, coconut oil, high-oleic sunflower oil, and single-cell oils (0.32% DHA; 0.64% ARA).

‡ Carbohydrate Source: Lactose from cow's milk. Also contains the prebiotic carbohydrates galactooligosaccharide and polydextrose.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Enfamil® Restfull™

20 Cal/fl oz

Available as powder.

Nutrient	per 100 Cal	per Liter
<b>Energy, Cal</b>	100	676
<b>Volume, mL</b>	148	1000
<b>Protein, g</b>	2.5	16.9
% of total calories †	10	10
<b>Fat, g</b>	5.1	34.5
% of total calories ††	46	46
Linoleic acid, mg	860	5811
Linolenic acid, mg	85	574
<b>Carbohydrate, g</b>	11	74.3
% of total calories ‡	44	44
<b>Water, g</b>	134	905
<b>Minerals</b>		
Calcium, mg	78 (3.9)	527 (26.4)
Phosphorus, mg	53 (1.7)	358 (11.6)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Iodine, mcg	10	67.6
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	40 (1.8)	270 (11.7)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	75 (2.1)	507 (14.2)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	60	405
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54.1
Thiamine B <sub>1</sub> , mcg	80	540
Riboflavin B <sub>2</sub> , mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6757
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20.3
Vitamin C, mg	12	81
Choline, mg	24	162
Inositol, mg	6	40.5
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
<b>Renal Solute Load, mOsm</b>	23	153
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	230	230
<b>Osmolarity, mOsm/L</b>	210	210

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk.

†† Fat Source: Palm olein oil, soy oil, coconut oil, high-oleic sunflower oil, and single-cell oil blend (3% DHA and ARA).

‡ Carbohydrate Source: Lactose, rice starch, and maltodextrin.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

## Pregestimil®

20 Cal/fl oz

Available as powder (P) and ready-to-feed (L).

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories †	11	11
Fat, g	5.6	37.9
% of total calories ††	48	48
Linoleic acid, mg	940	6354
Carbohydrate, g	10.2	69
% of total calories ‡	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	94 (4.7)	635 (31.8)
Phosphorus, mg (mEq)	52 (1.7)	352 (11.3)
Magnesium, mg	8 (P) 11 (L)	54 (P) 74 (L)
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	744 (19)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
<b>Vitamins</b>		
Vitamin A, IU	350 (P) 380 (L)	2365 (P) 2568 (L)
Vitamin D, IU	50	338
Vitamin E, IU	4	27
Vitamin K, mcg	12	81
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	90	608
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	2.03
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	168
Osmolality, mOsm/kg H <sub>2</sub> O	320 (P) 290 (L)	320 (P) 290 (L)
Osmolarity, mOsm/L	280 (P) 260 (L)	280 (P) 260 (L)

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Medium-chain triglyceride, soy, high-oleic vegetable oils, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Corn syrup solids and modified corn starch.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Pregestimil®**

24 Cal/fl oz

Available as ready-to-feed.

<b>Nutrient</b>	<b>per 100 Cal</b>	<b>per Liter</b>
<b>Energy, Cal</b>	100	813
<b>Volume, mL</b>	123	1000
<b>Protein, g</b>	2.8	22.8
% of total calories †	11	11
<b>Fat, g</b>	5.6	45.5
% of total calories ††	48	48
<b>Linoleic acid, mg</b>	940	7642
<b>Carbohydrate, g</b>	10.2	82.9
% of total calories §	41	41
<b>Water, g</b>	108	878
<b>Minerals</b>		
Calcium, mg (mEq)	94 (4.7)	764 (46.7)
Phosphorus, mg (mEq)	52 (1.7)	423 (13.5)
Magnesium, mg	11	89
Iron, mg	1.8*	14.6*
Zinc, mg	1	8.1
Manganese, mcg	25	203
Copper, mcg	75	610
Molybdenum, mcg	—	—
Iodine, mcg	15	122
Selenium, mcg	2.8	22.8
Sodium, mg (mEq)	47 (2)	382 (16.6)
Potassium, mg (mEq)	110 (2.8)	894 (23)
Chloride, mg (mEq)	86 (2.4)	699 (19.7)
<b>Vitamins</b>		
Vitamin A, IU	380	3089
Vitamin D, IU	50	407
Vitamin E, IU	4	32.5
Vitamin K, mcg	12	98
Thiamine (B <sub>1</sub> ), mcg	80	650
Riboflavin (B <sub>2</sub> ), mcg	90	732
Vitamin B <sub>6</sub> , mcg	60	488
Vitamin B <sub>12</sub> , mcg	0.3	2.4
Niacin, mcg	1000	8130
Folic acid (Folacin), mcg	16	130
Pantothenic acid, mcg	500	4065
Biotin, mcg	3	24
Vitamin C (Ascorbic acid), mg	12	98
Choline, mg	24	195
Inositol, mg	17	138
L-Carnitine, mg	2	16.3
Taurine, mg	6	49
Nucleotide fortification, mg	—	—
<b>Renal Solute Load, mOsm</b>	25	200
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	340	340
<b>Osmolarity, mOsm/L</b>	300	300

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Medium-chain triglyceride, soy, and high-oleic vegetable oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and modified corn starch.

Enfamil® Gentlease®

20 Cal/fl oz

Available as powder and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.3	15.6
% of total calories †	9	9
Fat, g	5.3	35.8
% of total calories ††	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.8	73
% of total calories ‡	43	43
Water, g	134	906
<b>Minerals</b>		
Calcium, mg (mEq)	82 (4.1)	554 (27.7)
Phosphorus, mg (mEq)	46 (1.5)	311 (10)
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	-	-
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	36 (1.6)	243 (10.6)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	63 (1.8)	426 (12)
<b>Vitamins</b>		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	9	61
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	140	946
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	2.0
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	-	-
Renal Solute Load, mOsm	21	140
Osmolality, mOsm/kg H <sub>2</sub> O	230	230
Osmolarity, mOsm/L	210	210

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Protein Source: partially hydrolyzed nonfat milk and whey protein concentrate (60% whey and 40% casein).

†† Fat Source: Palm olein, soy, coconut, high oleic sunflower oils, and single-cell oils rich in DHA and ARA.

‡ Carbohydrate Source: Corn syrup solids and lactose.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.



Enfaport™ with 84% of fat as medium chain triglyceride oil for infants with chyllothorax or LCHAD\*

30 Cal/fl oz

Available as ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1010
Volume, mL	99	1000
Protein, g	3.5	35
% of total calories †	14	141
Fat, g	5.4	54.5
% of total calories ††	45	454
Linoleic acid, mg	350	3535
Alpha-Linolenic acid, mg	50	505
Carbohydrate, g	10.2	103
% of total calories ‡	41	414
Water, g	83	838
<b>Minerals</b>		
Calcium, mg	94	949
Phosphorus, mg	52	525
Magnesium, mg	11	111
Iron, mg	1.8**	18**
Zinc, mg	1	10
Manganese, mcg	25	252
Copper, mcg	75	757
Iodine, mcg	15	151
Selenium, mcg	2.8	28
Sodium, mg (mEq)	30 (1.3)	303 (13.1)
Potassium, mg (mEq)	115 (2.9)	1161 (29.3)
Chloride, mg (mEq)	87 (2.5)	879 (25.3)
<b>Vitamins</b>		
Vitamin A, IU	350	3535
Vitamin D, IU	50	505
Vitamin E, IU	4	40
Vitamin K, mcg	12	121
Thiamin B <sub>1</sub> , mcg	80	808
Riboflavin B <sub>2</sub> , mcg	90	909
Vitamin B <sub>6</sub> , mcg	68	687
Vitamin B <sub>12</sub> , mcg	0.3	3
Niacin, mcg	1000	10101
Folic acid, mcg	16	162
Pantothenic acid, mcg	500	5050
Biotin, mcg	3	30
Vitamin C, mg	12	121
Choline, mg	24	242
Inositol, mg	17	172
Renal Solute Load, mOsm	28	290
Osmolality, mOsm/kg H <sub>2</sub> O	280	280
Osmolarity, mOsm/L	240	240

\* Long chain 3-hydroxyacyl-CoA dehydrogenase is a rare inherited disorder of fatty acid oxidation.

\*\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Calcium caseinate and sodium caseinate.

†† Fat Source: Medium chain triglyceride and soy oils, and 3% single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate source: Corn syrup solids.

**Nutramigen®**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories <sup>†</sup>	11	11
Fat, g	5.3	35.8
% of total calories <sup>††</sup>	48	48
Linoleic acid, mg	860	5813
Carbohydrate, g	10.3	69.6
% of total calories <sup>‡</sup>	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg (mEq)	94 (4.7)	635 (31.8)
Phosphorus, mg (mEq)	52 (1.7)	352 (11.3)
Magnesium, mg	11	74
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	744 (19.1)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2028
Vitamin D, IU	50	338
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	90	608
Vitamin B <sub>6</sub> , mcg	60	406
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	168
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	270	270

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Palm olein, soy, coconut, and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate Source: Corn syrup solids and modified corn starch.

**CAUTION:** This product is not recommended for routine use in very low-birth-weight infants. Some of these infants may be at increased risk of developing gastrointestinal complications.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Nutramigen® AA™ Hypoallergenic Amino Acid-Based Formula**

20 Cal/fl oz

Available as powder.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories †	11	11
Fat, g	5.3	35.8
% of total calories ††	48	48
Linoleic acid, mg	860	5811
Linolenic acid, mg	80	540
Carbohydrate, g	10.3	69.6
% of total calories ‡	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg	94	635
Phosphorus, mg	52	351
Magnesium, mg	11	74
Iron, mg	1.8*	12.2
Zinc, mg	1	6.8
Manganese, mcg	60	405
Copper, mcg	75	507
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	743 (19)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	50	338
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamin B <sub>1</sub> , mcg	80	541
Riboflavin B <sub>2</sub> , mcg	90	608
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6756
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20
Vitamin C, mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Renal Solute Load, mOsm	25	168
Osmolality, mOsm/kg H <sub>2</sub> O	350	350
Osmolarity, mOsm/L	320	320

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: 100% free amino acids.

†† Fat Source: Palm olein, soy, coconut, high-oleic sunflower oils, and 2.5% single-cell oil blend rich in DHA and ARA.

‡ Carbohydrate source: Corn syrup solids and modified tapioca starch.

**CAUTION:** This product is not recommended for routine use in very low-birth weight infants. Some of these infants may be at increased risk of developing gastrointestinal complications.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Nutramigen® Enflora™ LGG® Hypoallergenic Protein Hydrolysate Formula  
20 Cal/fl oz  
Available as powder.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories <sup>†</sup>	11	11
Fat, g	5.3	35.8
% of total calories <sup>††</sup>	48	48
Linoleic acid, mg	860	5811
Linolenic acid, mg	80	540
Carbohydrate, g	10.3	69.6
% of total calories <sup>‡</sup>	41	41
Water, g	133	899
<b>Minerals</b>		
Calcium, mg	94 (4.7)	635 (31.8)
Phosphorus, mg	52 (1.7)	351 (11.3)
Magnesium, mg	8	54.1
Iron, mg	1.8**	12.2**
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	743 (19.1)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
<b>Vitamins</b>		
Vitamin A, IU	300	2027
Vitamin D, IU	50	338
Vitamin E, IU	2	13.5
Vitamin K, mcg	9	60.8
Thiamine (B <sub>1</sub> ), mcg	80	541
Riboflavin (B <sub>2</sub> ), mcg	90	608
Vitamin B <sub>6</sub> , mcg	60	405
Vitamin B <sub>12</sub> , mcg	0.3	2
Niacin, mcg	1000	6757
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20.3
Vitamin C, mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Renal Solute Load, mOsm	25	168
Osmolality, mOsm/kg H <sub>2</sub> O	300	300
Osmolarity, mOsm/L	270	270

\*\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

<sup>†</sup> Protein Source: Hydrolyzed casein supplemented with L-cystine, L-tyrosine, and L-tryptophan.

<sup>††</sup> Fat Source: Palm olein oil, soy oil, coconut oil, high-oleic sunflower oil, and single-cell oil blend containing DHA and ARA.

<sup>‡</sup> Carbohydrate Source: Corn syrup solids and modified corn starch.

\* Probiotics: This formula contains *Lactobacillus rhamnosus* GG at a concentration of  $1 \times 10^8$  CFUs/g of powdered formula.

**CAUTION:** This product is not recommended for routine use in very low-birth-weight infants. Some of these infants may be at increased risk of developing gastrointestinal complications.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Good Start® Protect Plus®**

20 Cal/fl oz

Available as powder, concentrate, and ready-to-feed.

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	670
Volume, mL	148	1000
Protein, g	2.2	14.7
% of total calories †	9	9
Fat, g	5.1	34.2
% of total calories ††	46	46
Linoleic acid, mg	900	6030
Carbohydrate, g	11.2	75
% of total calories ‡	45	45
Water, g	134	900
<b>Minerals</b>		
Calcium, mg (mEq)	67 (3.3)	429 (21.5)
Phosphorus, mg (mEq)	38 (1.3)	241 (7.8)
Magnesium, mg	7	46.9
Iron, mg	1.5	10.1
Zinc, mg	0.8	5.4
Manganese, mcg	15	46.9
Copper, mcg	80	536
Molybdenum, mcg	—	—
Iodine, mcg	12	80.4
Selenium, mcg	2	13.4
Sodium, mg (mEq)	27 (1.2)	181 (7.8)
Potassium, mg (mEq)	108 (2.8)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	436 (12.3)
<b>Vitamins</b>		
Vitamin A, IU	300	2010
Vitamin D, IU	60	402
Vitamin E, IU	2	13.4
Vitamin K, mcg	8	54
Thiamine (B <sub>1</sub> ), mcg	100	670
Riboflavin (B <sub>2</sub> ), mcg	140	938
Vitamin B <sub>6</sub> , mcg	75	503
Vitamin B <sub>12</sub> , mcg	0.33	2.2
Niacin, mcg	1050	7035
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3015
Biotin, mcg	4.4	29.5
Vitamin C (Ascorbic acid), mg	9	60.3
Choline, mg	12	80.4
Inositol, mg	6	40.2
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	5	34
Renal Solute Load, mOsm	19	131
Osmolality, mOsm/kg H <sub>2</sub> O	250	250
Osmolarity, mOsm/L	—	—

† Protein Source: Enzymatically Hydrolyzed Reduced Minerals Whey Protein Concentrate (From Cow's Milk)

†† Fat Source: Vegetable oils (palm olein, soy, coconut, and high-oleic safflower or high-oleic sunflower), and C. cohnii<sup>1</sup> and M. alpina<sup>2</sup> oils.  
DHA and ARA are 0.32 and 0.64% of total fat.

<sup>1</sup> A source of docosahexaenoic acid (DHA).

<sup>2</sup> A source of arachidonic acid (ARA).

<sup>§</sup> Carbohydrate Source: lactose, corn maltodextrin.

Potential Allergens: Contains milk protein.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Neocate® Infant**

20 Cal/fl oz (see footnotes for preparation)

<b>Nutrient</b>	<b>per 100 Cal</b>	<b>per Liter</b>
<b>Energy, Cal</b>	100	676
<b>Volume, mL</b>	148	1000
<b>Protein, g</b>	3.1	20.9
% of total calories †	12	12
<b>Fat, g</b>	4.5	30.4
% of total calories ††	41	41
<b>Linoleic acid, mg</b>	677	4577
<b>Carbohydrate, g</b>	11.7	79.1
% of total calories ‡	47	41
<b>Water, g</b>	131	886
<b>Minerals</b>		
Calcium, mg (mEq)	124 (6.2)	838 (41.9)
Phosphorus, mg (mEq)	93	629
Magnesium, mg	12.4	83.8
Iron, mg	1.85*	12.5*
Zinc, mg	1.66	11.2
Manganese, mcg	90	608
Copper, mcg	124	838
Molybdenum, mcg	4.75	32.1
Iodine, mcg	15.4	104
Selenium, mcg	3.73	25.2
Sodium, mg (mEq)	37.3 (1.6)	252 (11)
Potassium, mg (mEq)	155.1 (4)	1048 (26.9)
Chloride, mg (mEq)	77.2 (2.2)	522 (14.8)
<b>Vitamins</b>		
Vitamin A, IU	391	2643
Vitamin D, IU	59.9	405
Vitamin E, IU	1.14	7.7
Vitamin K, mcg	8.79	59.4
Thiamine (B <sub>1</sub> ), mcg	92.6	626
Riboflavin (B <sub>2</sub> ), mcg	137.8	932
Vitamin B <sub>6</sub> , mcg	123.5	835
Vitamin B <sub>12</sub> , mcg	0.26	1.76
Niacin, mcg	1544	10437
Folic acid (Folacin), mcg	10.2	69
Pantothenic acid, mcg	620	4191
Biotin, mcg	3.1	21
Vitamin C (Ascorbic acid), mg	9.26	62.6
Choline, mg	13.1	89
Inositol, mg	23.3	158
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
<b>Renal Solute Load, mOsm</b>	28.5	192.6
<b>Osmolality, mOsm/kg H<sub>2</sub>O</b>	375	375
<b>Osmolarity, mOsm/L</b>	332	332

\* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: L-amino acids.

†† Fat Source: High oleic safflower oil (11%) and refined vegetable oil (coconut 6%, soy 3%).

‡ Carbohydrate Source: Corn syrup solids.

**Preparation (20 Cal/fl oz):**

Use one unpacked level scoop (4.75 g), enclosed, of powder for each fluid ounce of final volume of prepared formula. Add fluid to powder and adjust to 1 oz level.

**WARNING:** Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Medium Chain Triglyceride Oil**

Medium chain triglycerides (MCT) are lipid fractions of coconut oil consisting of triglycerides with chain lengths of 6 to 10 carbons. Used to supplement orally, or added to tube feeding formulas. Mixes easily with enteral formulas.

**MCT Oil**

Nutrient	per mL	per 15 mL (1 tbsp)	per 89 mL (3 fl oz)
Calories	7.7	115	685.3
Protein, g	0	0	0
Fat, g	0.94	14	44.5
Carbohydrate, g	0	0	0
Water, g	0	0	0
Linoleic Acid, g	0.367	5.5	32.63

**Fatty Acid Distribution**

Shorter than carbon 8	<6%
Caprylic C8:0	67%
Capric C10:0	23%
Longer than C10:0	<4%

**Osmolality (mOsm/kg water):** Not Available

**Supplied:** 1 quart glass bottles.

**Ingredients:** Medium chain triglycerides.

**For oral use only.** Do not give parenterally (IV). Use within 60 to 90 days after a bottle is opened. Do not store in plastic container. MCT may break or soften plastic containers.

Microlipid® is a 50% safflower oil fat emulsion with 4.5 Cal/mL. Used to supplement orally, or added to tube feeding formulas. Mixes easily with enteral formulas.

Nutrient	per mL	per 15 mL (1 tbsp)	per 89 mL (3 fl oz)
Calories	4.5	67.5	400
Protein, g	0	0	0
Fat, g	0.5	7.54	44
Carbohydrate, g	0	0.04	0
Water, g	0.45	6.7	40
Linoleic Acid, g	0.4	5.9	35

#### Fatty Acid Distribution

Polyunsaturated	78%
Monounsaturated	12%
Saturated	10%
PUFA:SFA	8:1

**Osmolality (mOsm/kg water):** Not available

**Supplied:** 48 three ounce bottles per case.

**Ingredients:** Safflower oil, water, polyglycerol esters of fatty acids, soy lecithin, xanthan gum, ascorbic acid.

**For oral use only.** Do not give parenterally (IV). Shake well before opening. Opened product should be recapped, refrigerated, and discarded after 5 days. Store unopened bottles at room temperature. Protect from freezing.



**Dose & Administration**

Begin at 0.5 g/kg per day IV increasing by 0.5 g/kg per day to a maximum of 3 g/kg per day. Infusion rate should not exceed 0.15 g/kg per hour. 24 hour infusion times are preferred. Essential fatty acid deficiency may be prevented with 0.5 to 1 g/kg per day.

**Fat Emulsion**

	Intralipid® 20%	Liposyn II® 20%	Liposyn III® 20%
<b>Oils (%)</b>			
Safflower	0	10	0
Soybean	20	10	20
<b>Fatty Acid Content (%)</b>			
Linoleic	50	65.8	54.5
Oleic	26	17.7	22.4
Palmitic	10	8.8	10.5
Linolenic	9	4.2	8.3
Stearic	3.5	3.4	4.2
Egg yolk phospholipid (%)	1.2	1.2	1.2
Glycerine (%)	2.25	2.5	2.5
Calories (per mL)	2	2	2
Osmolarity (mOsm/L)	260	258	292

**Uses**

Parenteral nutrition source of calories and essential fatty acids.

**Monitoring**

Monitor serum triglycerides (<200 mg/dL), liver function test, platelet count, albumin, glucose, and bilirubin.

**Adverse Effects/Precautions****Black Box Warning**

According to the manufacturer's black box warning, deaths due to intravascular fat accumulation in the lungs of preterm infants after infusion of IV fat emulsion have been reported. Strict adherence to the recommended total daily dose and hourly infusion rates is recommended. Infusion rates should not exceed 1 g/kg in four hours.

Hypertriglyceridemia and hyperglycemia. The minimum dose should be used in infants with severe hyperbilirubinemia, sepsis, or severe pulmonary dysfunction. Extravasation may cause tissue inflammation and necrosis.

**Pharmacology**

Intravenous fat emulsions are high caloric (2 Cal/mL) isotonic emulsions of either soybean or safflower oil. Fat particle size is between 0.4 and 0.5 microns in diameter, similar to endogenous chylomicrons. Clearance is via endogenous lipoprotein lipase activity, which is limited in very premature (<28 weeks gestation) and infected infants. Twenty percent emulsions are preferred due to lower total phospholipid and liposome content per gram of triglyceride. Ten percent emulsions have been associated with hypercholesterolemia and hyperphospholipidemia. Destabilization of lipid emulsions (flocculation and separation) may occur when they are co-infused with Dex/AA solutions containing calcium and high concentrations (>1 units/mL) of heparin. This risk may be decreased by 1) minimizing the contact time; 2) using low ( $\leq$  1 units/mL) concentrations of heparin; and 3) adding a multivitamin preparation to the Dex/AA solution.

**Special Considerations/Preparation**

Liposyn® and Intralipid® are available in 10% and 20% concentrations in 50, 100, 250, and 500 mL bottles. Store at room temperature

Do not freeze.

Use within 24 hours when dispensed in syringes.

There are no specific data regarding the compatibility of dobutamine or dopamine and fat emulsions. Dobutamine and dopamine are most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dobutamine or dopamine and fat emulsion together; dobutamine or dopamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

**Solution Compatibility:** D<sub>5</sub>W, D<sub>10</sub>W, and NS.

**Terminal Injection Site Compatibility:** Dex/AA. Aminophylline, ampicillin, aztreonam, bumetanide, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, digoxin, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, fluconazole, furosemide, gentamicin, heparin ( $\leq 1$  unit/mL), hydrocortisone, imipenem/cilastatin, insulin, isoproterenol, lidocaine, meropenem, metoclopramide, metronidazole, morphine, nafcillin, netilmicin, norepinephrine, oxacillin, penicillin G, piperacillin, piperacillin/tazobactam, potassium chloride, pyridoxine, ranitidine, sodium bicarbonate, sodium nitroprusside, ticarcillin, ticarcillin/clavulanate, tobramycin, trimethoprim/sulfamethoxazole, vancomycin, and zidovudine.

**Incompatibility:** Acyclovir, amikacin, amphotericin B, lorazepam, magnesium chloride, midazolam, octreotide acetate, pentobarbital, phenobarbital, and phenytoin.

**Selected References**

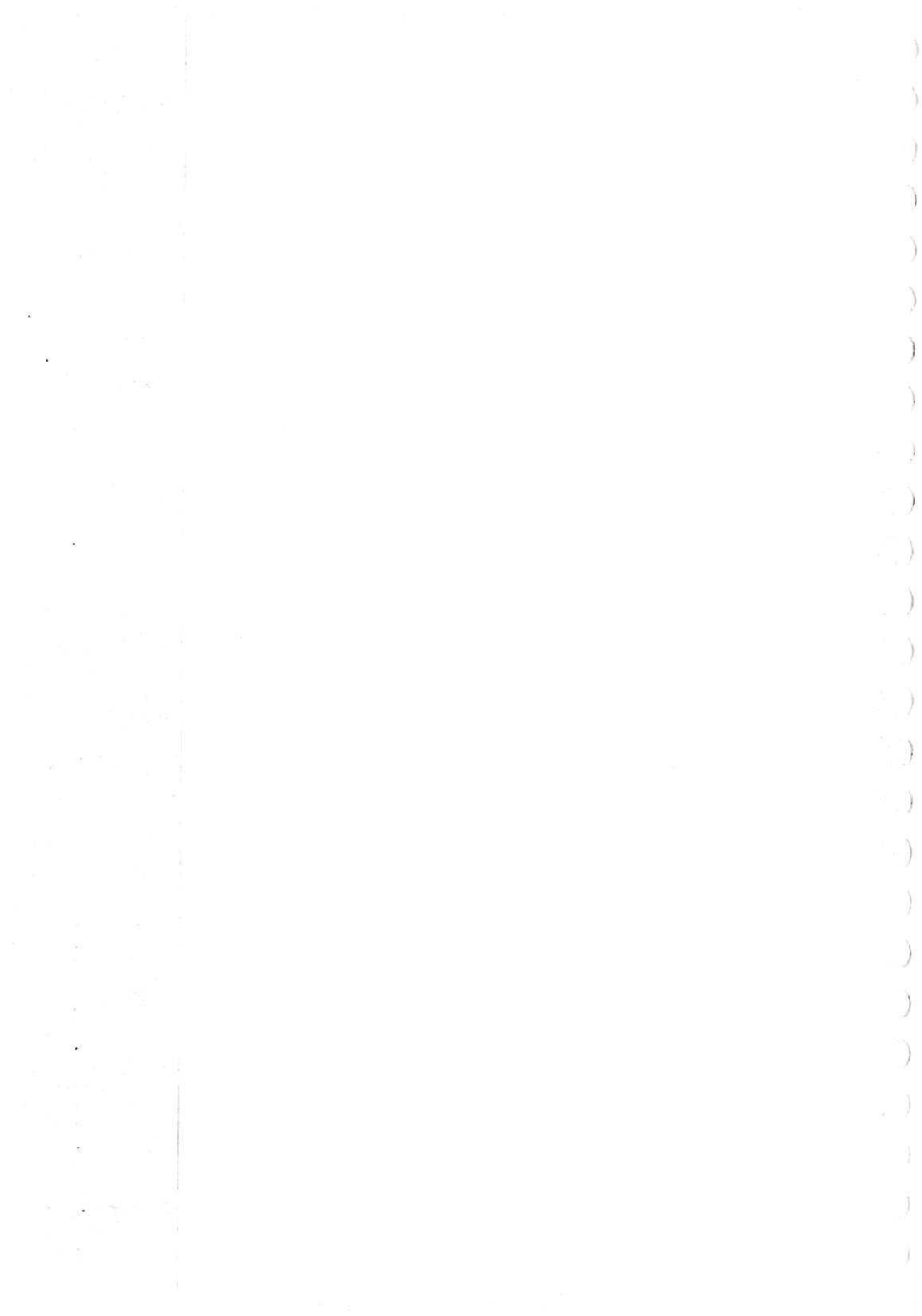
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Adverse Effects/Precautions updated 3/2009

Special Considerations updated 3/2008

Compatibility updated 3/2008

Added 3/1999



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**RECOMMENDED  
CONCENTRATIONS  
FOR  
ADMINISTRATION**

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430 Antimicrobials						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Acyclovir	IV	mg/mL	50*	7	7	5
Amikacin	IV	mg/mL	50*	10	10	5
Amikacin	IM	mg/mL	50	50	50	10
Amphotericin B	IV	mg/mL	5*	0.1	0.1	0.05
Amphotericin B Lipid Complex	IV	mg/mL	5*	2	2	0.5
Amphotericin B Liposome	IV	mg/mL	4*	2	2	1
Ampicillin	IV	mg/mL	125 or 250*	50	100	20
Ampicillin	IM	mg/mL	250	250	250	125
Azithromycin	IV	mg/mL	100*	2	2	1
Aztreonam	IV	mg/mL	100	20	20	10
Aztreonam	IM	mg/mL	125 or 250	167	333	83
Caspofungin	IV	mg/mL	5*	0.2	0.5	0.1
Cefepime	IV	mg/mL	100	100	160	100
Cefepime	IM	mg/mL	280	280	280	160
Cefazolin	IV	mg/mL	225*	100	125	20
Cefazolin	IM	mg/mL	225	330	330	100
Cefotaxime	IV	mg/mL	50 or 100	50	100	25
Cefotaxime	IM	mg/mL	230 or 300	300	330	100
Cefoxitin	IV	mg/mL	100*	40	100	20
Ceftazidime	IV	mg/mL	50	100	200	50
Ceftazidime	IM	mg/mL	200	200	200	50
Ceftriaxone	IV	mg/mL	40 or 100*	40	40	20
Ceftriaxone	IM	mg/mL	250	250	250	100
Chloramphenicol	IV	mg/mL	100 *	10	100	5
Clindamycin	IV	mg/mL	150*	10	18	6
Erythromycin Lactobionate	IV	mg/mL	50*	5	5	1
Fluconazole	IV	mg/mL	2	2	2	2
Ganciclovir	IV	mg/mL	50*	5	10	5
Gentamicin	IV	mg/mL	10	10	10	2
Gentamicin	IM	mg/mL	40	10	40	10
Imipenem - Cilastatin	IV	mg/mL	25 or 50	5	5	2.5
Linezolid	IV	mg/mL	2	2	2	2
Meropenem	IV	mg/mL	50	50	50	25
Metronidazole	IV	mg/mL	5	5	5	5
Micafungin	IV	mg/mL	10 or 20*	1	1.5	0.5
Nafcillin	IV	mg/mL	250*	40	40	20
Netilmicin	IM	mg/mL	100*	5	100	2.5
Oxacillin	IV	mg/mL	50	25	100	25

\* See Neofax Special Consideration/Preparation section for dilution details

NEOFAX® 2011

Antimicrobials						431
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Penicillin G	IV	U/mL	500,000	100,000	500,000	50,000
Piperacillin	IV	mg/mL	200	100	200	50
Piperacillin	IM	mg/mL	400	300	400	100
Piperacillin - Tazobactam	IV	mg/mL	200	50	200	20
Rifampin	IV	mg/mL	60*	3	6	3
Ticarcillin - Clavulanate	IV	mg/mL	200	50	100	10
Tobramycin	IV	mg/mL	10	10	10	2
Tobramycin	IM	mg/mL	40	40	40	10
Vancomycin	IV	mg/mL	50*	5	5	2.5
Zidovudine (ZDV, AZT)	IV	mg/mL	10*	4	4	2

Biologicals						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Epoetin alfa	IV	U/mL	2,000	2,000	4,000	2,000
Epoetin alfa	SC	U/mL	2,000	2,000	4,000	2,000

Cardiovascular						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Adenosine	IV	mcg/mL	3000*	300	3,000	300
Alteplase	IV	mg/mL	1	1	1	1
Amiodarone	IV	mg/mL	50*	2	6	2
Atropine	IV	mg/mL	0.05 to 1*	0.4	1	0.05
Digoxin	IV	mcg/mL	100*	10	100	10
Enalaprilat	IV	mcg/mL	1250*	25	50	25
Enoxaparin	IV	mg/mL	100	100	100	100
Esmolol	IV	mcg/mL	10,000	10,000	10,000	1,000
Hydralazine	IV	mg/mL	20*	1	1	1
Indomethacin	IV	mg/mL	0.5 to 1	0.5	1	0.5
Milrinone	IV	mcg/mL	1000*	200	200	50
Procainamide	IV	mg/mL	100	2	4	2
Propranolol	IV	mg/mL	1*	1	1	0.1
Prostaglandin E1	IV	mcg/mL	500*	10	20	10
Sodium nitroprusside	IV	mg/mL	25	0.1	0.2	.01

\* See Neofax Special Consideration/Preparation section for dilution details

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432 CNS						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Fentanyl	IV	mcg/mL	50	10	20	5
Fosphenytoin	IV	mg PE/mL	50	25	25	1.5
Fosphenytoin	IM	mg PE/mL	50	50	50	50
Lorazepam	IV	mg/mL	2 or 4*	0.4	2	0.2
Midazolam	IV	mg/mL	1 or 5*	0.5	1	0.5
Morphine	IV	mg/mL	0.5 to 50*	0.4	5	0.1
Pancuronium	IV	mg/mL	1 or 2	1	2	0.5
Pentobarbital	IV	mg/mL	50*	5	50	5
Rocuronium	IV	mg/mL	10	1	5	1
Vecuronium	IV	mg/mL	1*	0.4	1	0.1

Diuretics						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Bumetanide	IV	mg/mL	0.25*	0.125	0.25	0.05
Bumetanide	IM	mg/mL	0.25*	0.125	0.25	0.05
Furosemide	IV	mg/mL	10*	2	10	2
Furosemide	IM	mg/mL	10*	10	10	5

GI						
Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Cimetidine	IV	mg/mL	150*	15	15	6
Famotidine	IV	mg/mL	10*	1	4	0.2
Metoclopramide	IV	mg/mL	5*	0.1	1	0.1
Ranitidine	IV	mg/mL	1 and 25*	2	2.5	0.5

\* See Neofax Special Consideration/Preparation section for dilution details

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Respiratory						433
			Concentration			
Generic Name	Route	Units	Available	Default	High	Low
Aminophylline	IV	mg/mL	25*	5	25	5
Dexamethasone	IV	mg/mL	4 or 10	0.2	1	0.1

Miscellaneous						
			Concentration			
Generic Name	Route	Units	Available	Default	High	Low
Hydrocortisone succinate	IV	mg/mL	100	10	10	1
Insulin	IV	U/mL	100*	1	5	0.2
Levothyroxine (T4)	IV	mcg/mL	40 or 100	20	40	20
Octreotide Acetate	IV	mcg/mL	50	25	100	10

\* See Neofax Special Consideration/Preparation section for dilution details

NEOFAX® 2011





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# NEWBORN METRIC CONVERSION TABLES

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**Agustín Torres Mendoza**  
PEDIATRA NEONATOLOGO  
CMP. 27344  
RNE. 16790 - 19715  
JEFF DE OPTO. PEDIATRÍA

## Newborn Metric Conversion Tables

### Temperature in Fahrenheit (F) to Celsius (C)

°F	°C	°F	°C	°F	°C	°F	°C
93.2 ...	34.0	96.2 ...	35.7	99.2 ...	37.3	102.2 ...	39.0
93.4 ...	34.1	96.4 ...	35.8	99.4 ...	37.4	102.4 ...	39.1
93.6 ...	34.2	96.6 ...	35.9	99.6 ...	37.6	102.6 ...	39.2
93.8 ...	34.3	96.8 ...	36.0	99.8 ...	37.7	102.8 ...	39.3
94.0 ...	34.4	97.0 ...	36.1	100.0 ...	37.8	103.0 ...	39.4
94.2 ...	34.6	97.2 ...	36.2	100.2 ...	37.9	103.2 ...	39.6
94.4 ...	34.7	97.4 ...	36.3	100.4 ...	38.0	103.4 ...	39.7
94.6 ...	34.8	97.6 ...	36.4	100.6 ...	38.1	103.6 ...	39.8
94.8 ...	34.9	97.8 ...	36.6	100.8 ...	38.2	103.8 ...	39.9
95.0 ...	35.0	98.0 ...	36.7	101.0 ...	38.3	104.0 ...	40.0
95.2 ...	35.1	98.2 ...	36.8	101.2 ...	38.4	104.2 ...	40.1
95.4 ...	35.2	98.4 ...	36.9	101.4 ...	38.6	104.4 ...	40.2
95.6 ...	35.3	98.6 ...	37.0	101.6 ...	38.7	104.6 ...	40.3
95.8 ...	35.4	98.8 ...	37.1	101.8 ...	38.8	104.8 ...	40.4
96.0 ...	35.6	99.0 ...	37.2	102.0 ...	38.9	105.0 ...	40.6

**Note:** °C = (°F - 32) x  $\frac{5}{9}$ . Celsius temperature equivalents rounded to one decimal place by adding 0.1 when second decimal place is 5 or greater. The metric system replaces the term Centigrade with Celsius (name of the inventor of the scale).

### Body Mass to Body Surface Area Approximation

$$\text{BSA (m}^2\text{)} = (0.05 \times \text{kg}) + 0.05$$

Weight (kg)	Approximate Surface Area (m <sup>2</sup> )	Weight (kg)	Approximate Surface Area (m <sup>2</sup> )
0.4 .....	0.07	2.8 .....	0.19
0.6 .....	0.08	3 .....	0.2
0.8 .....	0.09	3.2 .....	0.21
1 .....	0.1	3.4 .....	0.22
1.2 .....	0.11	3.6 .....	0.23
1.4 .....	0.12	3.8 .....	0.24
1.6 .....	0.13	4 .....	0.25
1.8 .....	0.14	4.2 .....	0.26
2 .....	0.15	4.4 .....	0.27
2.2 .....	0.16	4.6 .....	0.28
2.4 .....	0.17	4.8 .....	0.29
2.6 .....	0.18	5 .....	0.3

# Newborn Metric Conversion Tables

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## Length in inches (in. ) to centimeters (cm)

**1-in. increments.** Example: To obtain centimeters equivalent to 22 in., read "20" on top scale, "2" on side scale; equivalent is 55.9 cm.

Inches	0	10	20	30	40
0	0	25.4	50.8	76.2	101.6
1	2.5	27.9	53.3	78.7	104.1
2	5.1	30.5	55.9	81.3	106.7
3	7.6	33.0	58.4	83.8	109.2
4	10.2	35.6	61.0	86.4	111.8
5	12.7	38.1	63.5	88.9	114.3
6	15.2	40.6	66.0	91.4	116.8
7	17.8	43.2	68.6	94.0	119.4
8	20.3	45.7	71.1	96.5	121.9
9	22.9	48.3	73.7	99.1	124.5

**1/4-in. increments.** Example: To obtain centimeters equivalent to 14 3/4 in., read "14" on top scale, "3/4" on side scale; equivalent is 37.5 cm.

Inches	10	11	12	13	14	15
0	25.4	27.9	30.5	33.0	35.6	38.1
1/4	26.0	28.6	31.1	33.7	36.2	38.7
1/2	26.7	29.2	31.8	34.3	36.8	39.4
3/4	27.3	29.8	32.4	34.9	37.5	40.0

Inches	16	17	18	19	20	21
0	40.6	43.2	45.7	48.3	50.8	53.3
1/4	41.3	43.8	46.4	48.9	51.4	54.0
1/2	41.9	44.5	47.0	49.5	52.1	54.6
3/4	42.5	45.1	47.6	50.2	52.7	55.2

**Note:** 1 in. = 2.54 cm. Centimeter equivalents are rounded one decimal place by adding 0.1 when second decimal place is 5 or greater; for example, 33.48 becomes 33.5.

## Fluid Volume in ounces (oz) to milliliters (mL)

1 fl oz = 29.57 mL

(oz) . . (mL)	(oz) . . . (mL)	(oz) . . (mL)	(oz) . . (mL)
0.5 . . . 14.8	3 . . . . 88.7	9 . . . 266.2	18 . . . 532.3
0.75 . . 22.2	3.5 . . . 103.5	10 . . . 295.7	20 . . . 591.5
1 . . . . 29.6	4 . . . . 118.3	11 . . . 325.3	22 . . . 650.6
1.25 . . 37.0	4.5 . . . 133.1	12 . . . 354.9	24 . . . 709.8
1.5 . . . 44.4	5 . . . . 147.9	13 . . . 384.5	26 . . . 768.9
1.75 . . 51.8	6 . . . . 177.4	14 . . . 414.0	28 . . . 828.1
2 . . . . 59.1	7 . . . . 207.0	15 . . . 443.6	30 . . . 887.2
2.5 . . . 73.9	8 . . . . 236.6	16 . . . 473.2	32 . . . 946.4

## Newborn Metric Conversion Tables

**Weight (mass) pounds (lb) and ounces (oz) to grams (g).** Example: To obtain grams equivalent to 6 lb, 8 oz read "6" on top scale, "8" on side scale; equivalent is 2948 g.

Oz	Pounds						
	0	1	2	3	4	5	6
0	0	454	907	1361	1814	2268	2722
1	28	482	936	1389	1843	2296	2750
2	57	510	964	1417	1871	2325	2778
3	85	539	992	1446	1899	2353	2807
4	113	567	1021	1474	1928	2381	2835
5	142	595	1049	1503	1956	2410	2863
6	170	624	1077	1531	1984	2438	2892
7	198	652	1106	1559	2013	2466	2920
8	227	680	1134	1588	2041	2495	2948
9	255	709	1162	1616	2070	2523	2977
10	283	737	1191	1644	2098	2551	3005
11	312	765	1219	1673	2126	2580	3033
12	340	794	1247	1701	2155	2608	3062
13	369	822	1276	1729	2183	2637	3090
14	397	850	1304	1758	2211	2665	3118
15	425	879	1332	1786	2240	2693	3147

Oz	Pounds					
	7	8	9	10	11	12
0	3175	3629	4082	4536	4990	5443
1	3203	3657	4111	4564	5018	5471
2	3232	3685	4139	4593	5046	5500
3	3260	3714	4167	4621	5075	5528
4	3289	3742	4196	4649	5103	5557
5	3317	3770	4224	4678	5131	5585
6	3345	3799	4252	4706	5160	5613
7	3374	3827	4281	4734	5188	5642
8	3402	3856	4309	4763	5216	5670
9	3430	3884	4337	4791	5245	5698
10	3459	3912	4366	4819	5273	5727
11	3487	3941	4394	4848	5301	5755
12	3515	3969	4423	4876	5330	5783
13	3544	3997	4451	4904	5358	5812
14	3572	4026	4479	4933	5386	5840
15	3600	4054	4508	4961	5415	5868

**Note:** 1 lb = 453.59 g; 1 oz = 28.35 g; 1000 g = 1 kg. Gram equivalents have been rounded to whole numbers by adding 1 when the first decimal place is 5 or greater.

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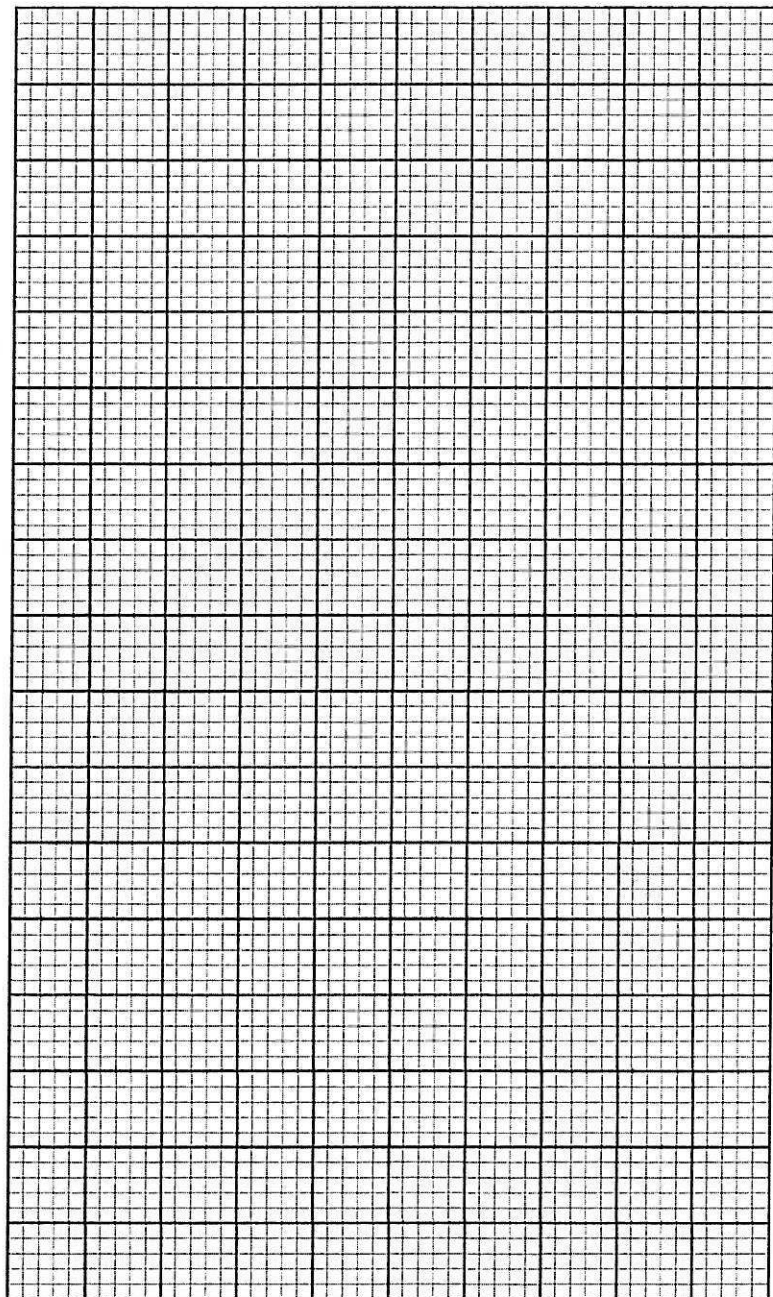


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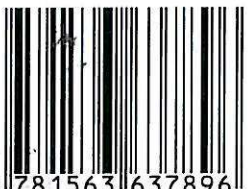
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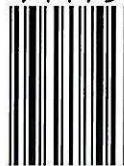
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